An evaluation of

ULTRASONIC FLOWMETRY

in vascular surgery

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To Judith

Für die Entwicklung der Lehre vom Kreislauf war es gewiß ein Verhängnis, dass das Strömvolumen verhältnismässig so umständlich, der Blutdruck aber gar so leicht bestimmbar ist: deshalb gewarm des Blutdruckmanometer einen geradezu faszinierenden Einfluß, obwohl die meisten Organe gar nicht Druck, sondern Strömvolumen brauchen.

Adolf Jarisch, (1928).
Kreislauffragen,
Deutsche Medizinische Wochenschrift, **54**: 1171-1173.

The development of our knowledge of the circulation has been hindered by the fact that the measurement of the blood flow volume is so complicated, whereas that of the blood pressure is so easy: the blood pressure manometer, as a result, has exerted an almost hypnotic influence, although most organs need blood flow, not pressure.

Preface and Acknowledgements

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Dr Judith Bell, who became my wife a few weeks before I submitted this work for examination, has given me unerring support and help throughout.

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Abstract

Although intraoperative flow measurement has long been used as a measure of successful arterial surgery, the use of volume blood flow in the routine examination and follow-up of patients with arterial reconstruction has not been reported. Modern duplex ultrasonic techniques provide information about morphology and hæmodynamics, including the measurement of volume blood flow, in a given blood vessel or bypass. The thesis aims to evaluate volume blood flow, both at rest and enhanced physiologically, as an objective index in postoperative patients with arterial reconstructions, comparing it with clinical and conventional non-invasive assessments.

The accuracy of the system, a Technicare Autosector scanner, was examined using *in vitro* techniques, and a linear response to blood flow over the tested range was confirmed. *In vivo* tests demonstrated that the measurements were reproducible. The normal lower limb blood flow was established in 58 limbs at rest, and the response to graded exercise studied in 6 normal volunteers. Enhancement of blood flow produced by a standard reactive hyperæmic test was compared with that produced by exercise testing in 18 patients with intermittent claudication.

Examination was made of 303 bypasses and bypass limbs in 210 patients. Real-time imaging allowed the identification of luminal irregularity and valve remnants in vein grafts. A tendency towards dilatation was demonstrated in knitted Dacron grafts, whereas the lumina of woven grafts were narrowed by tissue encroachment. In 85 femoropopliteal bypasses, flow measurements correlated well with symptoms, ankle pressure ratios and radiological demonstration of run-off. Hyperæmic flow proved a sensitive predictor of bypass failure. In 177 aortofemoral bypass limbs, flow measurements correlated with symptoms and run-off. Flow in 31 femorofemoral cross-over bypasses was significantly less than in 10 iliofemoral grafts, and, although usually asymptomatic, a steal of blood from the donor limb was demonstrated in most cases. In 118 carotid arteries, a luminal reduction of >75% was required before blood flow was reduced. The increase in blood flow following endarterectomy in 15 patients was

greater in those cases in whom a pressure gradient of >50 mmHg. was demonstrated at operation, but did not correlate with symptoms.

The measurements were generally easily performed, the results recommending the technique as suitable, not only for the purposes of clinical research, but also for routine use in the follow-up evaluation of patients with arterial reconstructions. The technique can confidently be recommended as the method of choice for the objective assessment of femoropopliteal bypass function.

Introduction

Purpose of the work

Although the follow-up assessment of patients after arterial reconstruction frequently rests on a clinical evaluation, and often on symptoms alone, the use of objective methods of hæmodynamic measurement has long been advocated. Resting ankle systolic blood pressure measurement, usually expressed as a ratio of brachial pressure, is the method most frequently employed, being simple to perform , versatile and reproducible. On the other hand, clinical blood flow measurement has, hitherto, been difficult and cumbersome, and the results difficult to interpret. Duplex ultrasonic scanners now provide a relatively simple means of measuring the volume of blood flow in a selected artery or arterial graft in an entirely non-invasive way, by computing the mean velocity of blood flow and combining this with measurements made from real-time images of the blood vessel under study. The technique offers an alternative approach, complementary to ankle pressure ratios and other non-invasive techniques, for quantifying the hæmodynamic state of the limb circulation. The purpose of the present thesis was to test the accuracy of such an instrument, the Technicare Autosector duplex scanner, and to evaluate its use in the routine follow-up of patients after arterial reconstruction to provide information which, in addition to that gained by clinical assessment and conventional non-invasive examination, might help further our understanding of how bypasses work, and to detect malfunction early so that failing grafts can be revived before they pass an irremediable stage.

Layout of the thesis

The background to the clinical measurement of blood flow is dealt with in Chapter One. The development of Doppler ultrasound and its clinical applications are described in Chapter Two, together with a discussion of the principles of measuring volume blood flow using ultrasonic techniques, and a theoretical analysis of the relative importance of each of the possible sources of error of the technique employed in the study. Chapter Three begins with a description of the apparatus and methods employed in the studies, and continues with a series of *in vitro* experiments designed to establish the accuracy of the ultrasound system in the measurement of blood flow, and *in vivo* tests of reproducibility.

The clinical studies which follow fall into three broad categories. In Chapter Four, normal values for lower limb blood flow are established and a standard reactive hyperæmia test is evaluated for use in conjunction with flowmetry studies. In the five subsequent chapters are set out the results of studies of postoperative patients who had undergone lower limb arterial reconstructions. Real-time ultrasound enabled a detailed examination of vein and fabric bypasses to be undertaken, the results of which are set out respectively in Chapters Five and Seven. Studies of patients with femoropopliteal reconstructions are described in Chapter Six, aortofemoral reconstructions in Chapter Eight and femorofemoral reconstructions in Chapter Nine. Chapter Ten consists of studies of the normal carotid circulation, and of the effect of stenosis and carotid endarterectomy on blood flow.

Although the data are discussed within their relevant chapters, a general discussion of the overall findings follows as Chapter Eleven. A general summary of the conclusions constitutes Chapter Twelve.

Chapter One

Background to flow measurement

Table 1.1

Milestones in blood flowmetry

1628	**Harvey**	*De Motu Cordis*
1733	**Hales**	*Haemastaticks*
1808	**Young**	Wave transmission in arteries
1842	**Poiseuille**	Flow of viscous fluids in narrow tubes
1842	**Doppler**	*Über das Farbige Licht der Doppelsterne*
1850	**Volkmann**	Measurement of blood flow per unit time
1860	**Chauveau**	Measurement of blood flow velocity using hydraulic pendulum
1870	**Fick**	Fick's Principle
1881	**Marey**	*Le circulation du sang à l'état physiologique et dans les malades* - Flow measurement using Pitot tube
1905	**Brodie & Russell**	Venous occlusion plethysmograph
1928	**Hamilton**	Measurement of human cardiac output using Fick's principle
1936	**Kolin**	Electromagnetic flow meter
1945	**Kety & Schmidt**	Measurement of cerebral blood flow using Fick's principle
1955	**Spencer**	Electromagnetic flowmeter applied to human renal artery
1960	**Satomura & Kanecko**	*Ultrasonic blood rheography*
1974	**Barber**	Duplex ultrasonic scanner

Historical background to blood flow measurement

The early years of the seventeenth century were those of a scientific renaissance in the form of a rapid progression from the dogmatic natural philosophy of the Middle Ages to the scientific methods of today, where argument is based on and supported by experimentation. Galileo, as Professor of Mathematics at Padua (1598-1610), represents the spirit of the age perhaps better than any other; it was to Padua that the young William Harvey (1578-1657) was attracted, in order to hear the lectures of the great anatomist Fabrizzi. In 1603, Fabrizzi published *De venarum ostiolis*, a great anatomical description of the venous valves which was a great inspiration to Harvey, who later made the crucial observation that the valves would allow passage of blood only in the direction of the heart. In his magnum opus, *Exercitatio Anatomica De Motu Cordis et Sanguinis in Animalibus* (1628), he proposed a circulation of the blood (*"Coepi egomet mecum cogitare, an motionem quondam quasi in circulo haberat"*), and established that arteries carry only blood, and not blood and air, and that their pulsations are passively driven by the action of the heart. His work aroused a storm of controversy, overturning, as it did, the sacrosanct teachings of Galen which, so logically and conveniently correlating with Greek humoral pathology, had been the traditional dogma of physicians for 1500 years.

The next major advances in arterial physiology were made over 100 years later by Stephen Hales (1677-1761), perpetual curate of Teddington. He was a great biological experimenter, and was well versed in the Newtonian concepts of force and velocity of flow. In his first book, *Vegetable Staticks* (1727), he investigated the forces required to raise sap to the top of very tall trees. His second book, *Haemastaticks* (1733), contains his great series of investigations of cardiovascular function. His most famous experiments were to measure the arterial and venous pressures in the horse, and to study the hæmodynamic effects of successive measured exsanguination. He measured the cardiac output in a human heart as 4.4 l/min. He deduced that the change from pulsatile arterial flow to venous flow was due to a smoothing action by the distensible properties of the arteries, acting as an elastic reservoir during ventricular systole. He also introduced the concept of peripheral resistance, and located the main site of this in the small vessels in the tissues.

The next developments which had an impact in this field were made in the field of material science. Leonhard Euler (1707-1783) developed his equations of fluid motion, and Daniel Bernoulli (1700-1782) wrote a treatise on hydrodynamics. Thomas Young (1733-1829) pioneered the study of the elastic properties of arteries in relation to pulse wave transmission and derived the basic equations relating pulse wave velocity to the properties of the elastic arterial wall.

Jean Léonard Marie Poiseuille (1799-1869), physician and physicist, applied both disciplines to further his understanding of the circulation. He used a U tube manometer, as Hales had done, filling it with mercury for measuring pressures in blood vessels, and confirmed that the main pressure drop occured in the arterioles. He subsequently published his study of the flow of viscous fluids in narrow tubes, using water, for he had no means of rendering blood incoagulable, and glass tubes of 140-300μ in diameter. He showed that the volume of blood flow was directly proportional to the pressure gradient and to the fourth power of the tube diameter, and inversely to the tube length.

Poiseuille's equation is theoretically applicable only to steady (i.e. non-pulsatile) laminar flow in a rigid tube of a fluid with Newtonian properties (i.e. with a viscosity which does not alter with the rate of shear). Although the cardiovascular system has none of these properties, the emphasis on radius and length highlighted by Poiseuille's results have helped our understanding the hæmodynamic effects of arterial stenoses.

Volkmann (1818-1864) was the first to measure blood flow per unit time in an artery. He devised, in 1850, a primitive method of measuring blood flow by introducing a U-shaped glass tube into the course of an artery.

In 1881, E. H. Marey published his textbook "*Le circulation du sang à l'état physiologique et dans des maladies*", in which he describes contemporaneous work on the measurement of pulsatile blood flow velocity. Both his own work, using a Pitot tube (*vide infra*) and that of Chauveau, using a hydraulic pendulum, produced blood flow velocity waveforms from peripheral arteries which resemble closely those accepted as normal today.

Flow meters based on the hydraulic pendulum

If a pendulum is freely suspended in a liquid then flow within the liquid will cause the pendulum to move. The force exerted on the pendulum results from friction and mass inertia of the fluid. Castelli (1577-1644) used such a device to measure the flow velocity of mountain streams. The first successful "haemodrometer" was used by Chauveau *et al* in 1860, permitting continuous recording of blood velocity. Later versions have improved on the technique by the introduction of electronics (Holzlöhner, 1938), and by the use of a flexible bristle as a pendulum (Bergmann, 1937; Brecher, 1954).

The bristle flowmeter has the advantages of offering minimal resistance to flowing blood and to demonstrate forward and backward flow equally well, although the effect of gravity on the bristle has to be considered. The technique shares the disadvantages shared by many of the invasive methods described, in that the blood vessel has to be opened and anticoagulants used; moreover, the calibration curve is non-linear.

Flowmetry using Bernouilli's theorem

Bernouilli, as mentioned earlier, related the velocity of an "ideal fluid", flowing in a horizontal tube, to the lateral pressure. This effect has been applied to two different sorts of flow meter, the orifice meter (Brömser, 1928; Shipley *et al*, 1943) and the Pitot tube flow meter. The latter, which has been the more widely applied (for example, in the measurement of airspeed in aircraft), was used by Marey, in 1881, who obtained excellent flow tracings demonstrating the reverse flow phase in femoral and carotid arteries.

Two major problems arise from the use of the Pitot meter. The first is that the presence of the tube within the vessel lumen creates eddies, and thus distorts the measurement of intraluminal pressure. The second problem relates to the fact that the velocity measured is that at a point on the cross section and not the mean velocity. In other words, the velocity profile must be known if accurate flow measurements are to be made.

Fick's Principle

Fick's principle (1870), relating blood flow to the ratio of the amount of the amount of an injected substance to its concentration in the effluent blood, was applied to the measurement of cardiac output in man by Hamilton *et al* in 1928. The principle, which can be applied to the measurement of blood flow in any organ or circulation in which the rate of blood clearance of a marker and the difference in concentration of the marker between arterial inflow and venous outflow may be measured, has been used to measure the blood flow in regional circulations, including the coronary blood flow (Hirche and Lockner, 1962), renal (Lockner and Ochwadt, 1954) and forearm blood flow (Andres *et al*, 1954). Kety and Schmidt, in 1945, used nitrous oxide washout to measure the cerebral circulation. In a subject breathing 15% nitrous oxide for 10 minutes, N_2O concentration analyses were performed on blood samples taken from the internal jugular vein and a peripheral artery.

Venous occlusion plethysmography

Brodie and Russell first described this method of measuring the blood flow to a limb (or to an organ which may be isolated and enclosed in a plethysmometer) in 1905. Whitney, in 1953, modified the technique by sustituting a mercury strain gauge for the air plethysmograph. This instrument has, in turn, been modified electronically to allow E.C.G. synchronisation and continuous monitoring.

Although Brodie and Russell, in their original paper, were aware of one of the main problems, that is "the venous occlusion must not be maintained so long as to impede capillary flow", the technique is relatively easily performed and, providing a non-invasive method of measuring mean limb blood flow, is therefore of clinical value.

Bubble Flowmeter

In 1934, Soskin described a flow meter, the principle of which is the timed passage of a bubble, completely filling the lumen of a glass tube of known calibre inserted into an artery, between two platinum electrodes. The flowmeter has subsequently been adjusted to allow continuous flow measurements to be made by the introduction of of a bubble injector at the proximal end of the tube and a bubble trap distally.

Blood flow measurement using indicator dilution

In 1949, Kety measured the disappearance of locally injected radioactive sodium chloride as an indicator of regional blood flow in skeletal muscle. Subsequently, using ^{133}Xe-labelled saline as a tracer, Lassen *et al*, in 1965, noted good correlation between maximum flow as determined by venous occlusion plethysmography and muscle blood flow as measured by indicator clearance. This method enabled dynamic blood flow measurements to be performed on patients with arterial disease, both at rest and during exercise. The technique is limited by its reproducibility, Lassen quotes a 25% coefficient of variation, and by the units of blood flow which are, of course, expressed as volume of blood per unit volume of tissue per unit time.

Electromagnetic flowmetry

The advent of electromagnetic flow devices marked a turning point in cardio-vascular measurement. Although the the methods of flowmetry it replaced were accurate, they were, on the whole, clumsy and disruptive.

The electromagnetic flow meter brought several advantages:

1. The blood vessel under study is left unopened and anticoagulants are not required
2. Interference with blood flow is minimal

3. There is direct transformation of the mechanical magnitude into an electrical signal.
4. The sensitivity both to forward and backward flow enables mean flow to be calculated
5. Calibration curves are linear
6. Calibration in terms of average velocity of flow rate is independent of the velocity profile and of the density, viscosity and temperature of the fluid.
7. The range of the frequency response is theoretically unlimited.
8. The technique is applicable to any electrically conductive fluids.

The meter uses the principle of magnetic induction to measure blood flow. Faraday, who had first demonstrated electromagnetic induction in solids and liquids, attempted in 1832, unsuccessfully to measure such an induced voltage created by the flow of the river Thames moving in the earth's magnetic field. The electromagnetic flowmeter was independently developed by Kolin, 1936, and by Wetterer, in 1937.

The electromagnetic flow meter was first applied to the human renal artery during a surgical operation by Spencer in 1955. By the 1960s, electromagnetic techniques had gained wide application to clinical measurement. Flow measurements were made at operation in lower limb (Cannon *et al*, 1960; Cappelan and Hall, 1964; Golding and Cannon, 1966; Mannick and Jackson, 1966) and carotid vessels (Hardesty *et al*, 1961, Kristianen and Krog, 1962) and renal artery (Hunt *et al*, 1965; Feezor and Boyce, 1965) amongst many other sites. Flow measurements made immediately after arterial reconstruction were related to the likelihood of a successful clinical outcome (Cappelan and Hall, 1967; Terry *et al*, 1972; Dedichen, 1967a). The changes in blood flow during the first few days after arterial reconstruction have also been measured, using a small flow transducer implanted at the time of surgery. (Cappelan and Hall, 1967; Cronestrand and Elekström, 1970; Samnegård and Elekström, 1974).

A disadvantage of the electromagnetic flowmeter is the need arrest the circulation in the vessel under study in order to determine its zero;

in the proximal aorta or pulmonary artery, for example, this cannot easily be achieved.

Other factors may lead to inaccurate or unreliable flow measurement.

1. Although the output of the flowmeter is independent of the velocity profile, this assumes that the flow is symmetrical about the axis of the blood vessel. If the velocity profile is skewed, then the flowmeter will give a false reading. Problems arise when the probe is placed close to a junction or atheromatous plaque.
2. The probe must fit the vessel snugly to ensure adequate electrical contact. The probe should have an internal diameter very slightly less than that of the blood vessel.
3. An increase in the hæmatocrit results in a slightly decreased flow signal, and *vice versa*, provided the hæmatocrit lies within the physiological range.
4. An abnormally thick vessel wall may give abnormally low results. Certain prosthetic materials, notably polytetrafluoroethylene, make flow values difficult to measure by electromagnetic means, because of air trapped within the interstices of the material.

Despite these factors, the electromagnetic flowprobe remains the method of choice for the measurement of flow within an exposed blood vessel, both intraoperatively and in experimental animal work. Electromagnetic flowmetry is used as a gold standard in the calibration of other flowmeters. A limitation of the technique for clinical use is that the flow-probe must be applied intraoperatively to the exposed artery. It cannot be used for diagnostic purposes, or for the purposes of monitoring a patient who has undergone an arterial reconstruction.

Chapter Two

Flow measurement using Doppler ultrasound

Introduction

The advent of Doppler ultrasound techniques has made possible the measurement of blood flow in a given vessel in an entirely non-invasive way, and has made it feasible to use flowmetry for routine assessment and follow-up of patients with certain arterial disorders. The simplest Doppler ultrasound devices are to be found in every arterial surgical clinic in the form of blood flow detectors. Instruments of far greater complexity based upon the analysis of Doppler shifted ultrasonic are now available, usually combined in a duplex scanner with an ultrasonic imaging system, offering an alternative approach to the assessment and follow-up of patients with vascular problems, and complementing more established techniques.

The purpose of the present chapter is to put the ultrasonic flowmeter into context. After a brief outline of the Doppler effect and its application to ultrasound, the different types of ultrasonic blood velocimeter are described. Different approaches to the measurement of volume blood flow are described, and the factors which determine the accuracy of the technique employed in the thesis are then discussed in some detail.

Historical aspects

Johann Christian Doppler's famous paper "On the coloured light of double stars and some other heavenly bodies" was given before the Royal Bohemian Society of Learning in 1842 and published the following year, whilst he was Professor of Elementary Mathematics and Practical Geometry at the State Technical Academy in Prague. In this famous work, Doppler recapitulated that the colour perceived by an observer varies with the frequency of the light, and proposed that the observed frequency will increase if the observer is moving towards the source of the light wave, and decrease if moving away. He explained this effect by analogy with a ship moving to meet or to retreat from a train of ocean waves.

One of his most vociferous critics was Buys Ballot, who, in 1845, tested the hypothesis experimentally, using sound waves. This he did in a novel way using two trumpeters, each playing a note of a given pitch. One trumpeter rode on a railway wagon whilst the other stood by the railway. An observer, who had perfect pitch, observed that, as the train approached, the sound of the trumpet on board was a semitone higher than the note sounded by the trumpeter on the ground, and a semitone lower after the train had passed. As the speed of the train had been about 40m.p.h., the observations correspond well with what would have been predicted from the Doppler equation, and the experiment may be regarded as the first recorded experimental verification of the acoustic Doppler effect.

It was not until the present century that the Doppler effect found scientific application. In 1929, Hubble showed that the more distant a galaxy the greater is the Doppler spectral shift toward the red, indicating increasing velocity of recession with distance, and thus established the modern concept of the expanding universe. The optical Doppler shift has found numerous other applications in astronomy, high temperature measurement and in aerial navigation using radio waves. A practical application of the acoustical Doppler effect was slower to emerge, and had to await the submarine detection methods used in World War II and development of ultrasonic techniques which followed.

Ultrasonic Doppler shift blood flowmetry

The ultrasonic Doppler shift blood velocimeter was first described by Satomura in 1959 and blood flow volume was measured using this technique by Franklin *et al* in 1961. Rushmer and his colleagues (1966) were the first to describe the measurement of blood flow velocity by measuring Doppler shifted ultrasound through intact skin. Clinical applications were soon to follow, notably for the study of peripheral vascular problems by Strandness and his colleagues in 1966.

A high frequency sound wave, in the order of 2 to 10 megaHerz, emitted from a transmitting piezo-electric crystal, oscillating at its natural frequency, is incident on moving red cells within the blood vessel. The wave is scattered in all directions by the blood cells; those backscattered waves which are detected by a receiving crystal will be of an altered frequency, according to the Doppler effect. The received frequency of this echo will be increased if the blood is moving towards the transducer, and decreased if the movement is away. The difference in frequency between the emitted and received ultrasound, or Doppler shift frequency, is usually within the audible spectrum and is proportional to the velocity of the blood cells.

In a system such as this, two frequency shifts occur. The first occurs between the emitting crystal and the moving blood cells, acting as receivers of ultrasound. A further shift in frequency of the scattered waves occurs between the blood cells and the receiving crystal (see Appendix I).

Ultrasonic velocimeters are broadly of two types, according to whether they employ continuous wave or pulsed (range-gated) Doppler ultrasound.

Continuous wave ultrasound

The transducer of a continuous wave Doppler contains two crystals, one transmitting ultrasound continuously and the other continually receiving. The familiar hand held Doppler flow detector represents the simplest form of this technology, in which the Doppler shifted frequencies are converted to an audible output which is appraised subjectively. In more sophisticated systems, the Doppler shift is represented graphically, as a directional velocity/time continuous display, and permitting qualitative or quantitative analysis. The disadvantage of such a system is that all moving objects in the path of the emitted ultrasound will cause frequency shift and clutter the signal from the blood vessel under study.

Pulsed wave ultrasound

Pulsed Doppler flow meters were developed in order to overcome the problem of the separation of flow signals of interest from those of adjacent arteries and veins (Fish, 1972; Mozersky *et al*, 1972). These systems employ only one crystal, which acts alternately as an emitter of a short pulse of ultrasound, and then as a receiver for the returning signals. Only those signals returning to the transducer during a pre-set period of time are processed. This so called "sample volume" will correspond to a certain area of tissue, the size, position and depth of which may be controlled by varying the pulse repetition frequency (P.R.F.). In order to provide a continuous wave form trace, rather than a discontinuous series of wave segments, the P.R.F. has to be at least twice as great as the Doppler frequency to be measured. This requirement tends only to be a problem if very fast flowing blood in a deep sited vessel is studied. Pulsed Doppler enables selection of those shifted frequencies from a particular anatomical location, thus eliminating extraneous noise from the Doppler signal, for example from blood flowing in adjacent veins. In modern duplex scanners like the Technicare Autosector, the gate size of the sample volume may be adjusted, in order to sample Doppler shifted frequencies from the whole lumen of the vessel under study.

B-mode ultrasound

A B-scan is an ultrasound tomogram which can be produced in any plane. The resulting two-dimensional image is spatial in both dimensions. By oscillating the transducer, a real-time image is produced. Ultrasonic imaging has gained wide acceptance, being the investigation of first choice for the pregnant uterus, gall-stones and aortic aneurysms, and used to provide images of carotid blood vessels, ovaries, testes, prostate and thyroid amongst other applications. Application of the technique is limited by the limits of penetration by ultrasound; almost complete reflection occurs at soft tissue-bone and soft tissue-air interfaces, preventing useful imaging through bowel gas or skull, for example. The frequency of the ultrasound will also determine its penetration; a lower frequency beam will penetrate more deeply, but at the expence of impaired resolution.

Duplex ultrasonic scanners

Duplex systems were designed in order that accurate positioning of the sample volume be made possible by combining the pulsed Doppler system with a high resolution B mode real-time imaging system in the same transducer head (Barber *et al*, 1974). In such systems, the angulation of the Doppler beam is shown, together with the depth and size of the sample volume (see figure 3.2). Although the system was initially designed so that the B mode system provided an accurate means of localising the Doppler sample volume, it has been recognised that the real-time image provides important information about the morphology of blood vessels, bypass grafts and atheromatous plaques.

The earliest duplex instruments consist of a Doppler velocimeter and an echo ultrasonic imaging system used to position the Doppler beam within the lumen of the blood vessel. The Doppler shift signal could be appraised using peak frequency measurement or spectral analysis. Later, the great importance of a good quality image of the blood vessel under examination led to the use of high resolution B-mode systems providing fast image acquisition. The provision of such a facility provides a stable reference platform for the Doppler measurements, allowing them to become fully quantitative, as opposed to the semi-quantitative or subjective methods of analysis which had been available hitherto. Although in many systems it has been necessary to record signals for later analysis, in some recent instruments, including the Technicare Autosector, a further refinement is provided in the form of an on-line computer. This permits instantaneous analysis of Doppler shift signals and measurement of the velocity of blood flow from the peak or mean frequency envelopes, and of the volume of blood flow using measurements made from the B-mode image.

Analysis of the Doppler shift spectrum

A single frequency Doppler shift will only be produced by a plane target moving at constant velocity through a uniform and infinitely wide ultrasonic field. Flow in a blood vessel shows a velocity profile across the lumen, so that the Doppler signal will be a spectrum of shift frequencies rather than a single frequency. Moreover, an ultrasound beam of finite width will undergo modulation both of frequency and amplitude when reflected by a target moving at uniform velocity. The signal received by the transducer will contain a spectrum of Doppler shift frequencies, resulting from this amplitude modulation of a waveform of single frequency.

Spectral broadening

Blood flow is laminar with a parabolic distribution of velocities only in straight and regular, non-branching blood vessels, which are circular in cross section and free from disease. Where the vessel lumen is narrowed or irregular the laminar pattern of blood flow will be disturbed by turbulence, and the spectrum of Doppler shift frequencies will be broadened.

Spectral analysis

In order to gain the maximum of information about blood flow, a system of analysis is required which will take into account the whole spectrum of flow velocities. This is based on a fast Fourier transform, whereby the the Doppler shift signal is resolved into 128 frequency components. Each of these represents a single Doppler shift frequency, which is proportional to one of the blood flow velocities present in the blood vessel. In a real-time system the transformation is repeated 100 times every second, the components of the analysis being displayed as a series of dots on the ordinate of a velocity/time display; the intensity of each dot is proportional to the amount of blood flowing at each particular velocity. A simultaneous computation of the maximum, modal or mean frequency shift permits a display of velocity/time curves in real-time.

Measurement of the volume of blood flow (see Appendix II)

Three approaches have been used to measure blood flow using Doppler ultrasonic techniques.

Flowmetry using assumed velocity profile

This simplest method has been used by several authors (Fisher *et al*, 1983: Huntsman *et al*, 1983) for the determination of cardiac output by measurement of blood flow through the ascending aorta or mitral valve. The blood in these situations is subject to great acceleration, and may be assumed to have a flat velocity profile. A Doppler shift maximum frequency sampled from any point over the vessel cross section is taken as the overall blood velocity. The angle of interrogation of the Doppler beam is assumed to be 0°, and the vessel cross-sectional area is estimated using an ultrasonic technique or even measured from an angiogram. Blood flow is the product of velocity and cross-sectional area.

This method is clearly less accurate than those in which the velocity profile is measured or taken into account, and is limited to those situations described in which blood flow approximates to a flat velocity profile.

Flowmetry using velocity profile measurement

In this method the blood vessel cross-section is considered as comprising a number of area elements, each representing blood moving at a particular velocity. The total blood flow is measured by summation of the flow contributions from all the elements of the cross-section area, each of which is calculated separately. Since the technique depends upon the measurement of blood velocity at each of a number of points across the vessel cross-section, a high spatial resolution pulsed Doppler beam is clearly required.

Usually, a multigated pulsed Doppler unit measures velocity at several points across the diameter of a vessel. The vessel is assumed to be circular, and the velocity profile to exhibit radial symmetry. The blood flow is calculated as the summation of each of the several flow components given by the product of each vector velocity (v_i) and its corresponding semiannular area (ΔA_i).

The technique is limited by the need for high resolution, which means that the sample volume of the pulsed Doppler beam must be very small in relation to the blood vessel diameter (Jorgensen, 1973; Baker D.W. *et al*, 1978; Fish, 1981). Baker concluded that the technique, lent itself best to the the measurement of flow within vessels greater than 1 cm in diameter.

Flowmetry using uniform insonation

This method enables the calculation of blood flow from the product of the vessel cross-sectional area and the spatial blood flow velocity averaged over the whole cross-section. The sample volume of the Doppler beam must encompass the whole cross-section of the vessel and should be uniformly sensitive so that ultrasound will be scattered proportionately from all points across the blood vessel cross-section. If this be assumed, the mean Doppler shift (Δf) is related to the spatial mean velocity ($\bar{v}$) by the Doppler equation as derived in Appendix I:

$$\Delta f = 2(\bar{v}.\cos\theta).\ f_o/c$$

But the volume of blood flow, Q, is the product of v and cross-sectional area, A:

$$Q = A.\ \bar{v} = \frac{A.\ \Delta f.\ c}{2f_o.\cos\theta}$$

This method is the most versatile of those described, being applicable to flow measurement in both superficial and deep vessels over a range of luminal calibres. It is the method employed in the Technicare Autosector duplex scanner used in the present study. The technique has been applied to the measurement of blood flow in the abdominal arteries (Qamar *et al, 1985; Aldoori et al*, 1985), portal vein (Gill, 1979; Nimura *et al*, 1983), and fetal umbilical vein (Gill, 1979; Eik-Nes *et al*, 1980).

Uniform insonation- accuracy and sources of error

Flow measurement using the method of uniform insonation depends upon the accurate measurement of blood vessel cross-sectional area and of the angle, θ, subtended by the ultrasound beam with the moving blood. The computation of mean blood flow from the Doppler shift frequency spectrum depends upon receiving scattered ultrasound uniformly from all points across the vessel lumen.

Estimation of the blood vessel cross-sectional area

If the blood vessel has a circular cross-section then the easiest method is to measure the luminal diameter, d, so that the area is given by:

$$A = \pi.d^2/4.$$

The Technicare scanner used in this thesis has a pulsed echo real-time B-mode ultrasound system. An incident beam produces sharpest echoes of the shortest direction and greatest amplitude at an angle of 90°, although a more acute angle is generally required. Luminal diameter may be measured using a pulsed Doppler beam by measuring the depth of field from which flow signals may be detected.

The variation of blood vessel diameter with time constitutes a possible source of error for flow measurement. The mean arterial diameter may first be measured over the cardiac cycle, using a M-mode scan, for example, and the mean value used for the flow calculation. Alternatively, the average of perhaps five measurements of diameter may be used for the calculation.

The calculation of cross-sectional area from diameter measurement clearly assumes a circular section. It is important to check that the diameter is circular from a cross-sectional image of the blood vessel obtained in a plane perpendicular to the longitudinal axis of the blood vessel. In the event of a non-circular lumen, many duplex scanners, including the Technicare Autosector, incorporate a facility for measurement of the area by moving a cursor around the lumen in a magnified frozen B mode image of the blood vessel cross-section.

Angle of approach

Accurate measurement of angle θ is required, not only for the estimation of blood velocity (Appendix I), but also for the accurate measurement of vessel diameter (Gill, 1982).

Errors in the calculation of blood flow arising from inaccuracies in the measurement of θ will be least when θ is as acute an angle as possible. In practice it is almost impossible to obtain an angle of approach of less than 40^o, but a small inaccuracy in θ measurement will result in an unacceptibly high percentage error in flow calculation if θ is greater than about 70^o. In the present study it has been found that flow measurements are most reproducible when $\theta \leqslant 55^o$, and all measurements of flow in which θ was $>60^o$ have been rejected.

It has been found most satisfactory to measure vessel diameter or cross-sectional area using a pulse echo beam incident at 90^o to produce a real-time image of least distorted quality, and then to readjust the image so that flow signals can be sampled from this chosen point at a more acute angle θ.

The angle of approach, θ, will not be estimated correctly if the blood vessel under interrogation does not lie precisely in the plane of the ultrasound scan, but cuts it at an angle ψ. This error is most likely to be encountered in deeply situated curved vessels or grafts. In this event, flow calculations will be underestimated, as the measured angle, θ', will be an underestimation of the true θ, that is:

$$\cos \theta = \cos \theta' . \cos \psi \quad \text{(Gill, 1985).}$$

Fortunately, the angle ψ is likely to be small; provided $\psi \leqslant 15^o$, the resulting underestimation of flow will not exceed 3%.

<u>Non-uniform scattering of ultrasound</u>

Flow measurement by this method assumes that scattered ultrasound is received uniformly from all points across the vessel lumen. Various factors may compromise this, however (Gill, 1982):

1. Non-uniform scattering by the blood due to non-uniform distribution of scatterers.
2. Non-uniform interrogation of the blood vessel by the ultrasound, due to non-uniform distribution within the sample volume
3. Non-uniform sensitivity function for the receiving transducer.

The non-uniformity of ultrasound scatters in the blood, that is the red blood corpuscles, is probably only a problem during turbulent blood flow; normally the red cell density is uniform across the blood vessel, except for the most peripheral layers. The non-uniformity of ultrasound density within the sample volume and the sensitivity of the receiving transducer are problems of ultrasound technology and scanner design and, being dealt with elsewhere (Gill, 1982) will not be considered further. Any problems of this type will doubtless be improved in later generations of ultrasound scanner. Non-uniform interrogation of the blood vessel due to incomplete insonification can be minimised by using as large a sample volume as possible in order to ensure that it spans the whole width of the blood vessel. The beamwidth should, ideally, be slightly greater than the blood vessel diameter. Errors of upto 22% may result from the use of too narrow a beamwidth.

It is difficult to predict the overall effects of these theoretical sources of error. A series of experiments was therefore performed in order to test the accuracy of the Technicare Autosector duplex scanner. These will be described in the next chapter, following a brief description of the apparatus.

Chapter Three

The Technicare Autosector duplex ultrasonic scanner and its experimental validation

Introduction

The Technicare Autosector (figure 3.1), used for the studies described in this thesis, represented the most recent technology in the field of ultrasonic duplex scanners at the time the studies were performed (1984/85). The instrument combines a high resolution real-time imaging system of 7.5 or 10 MHz with a Doppler velocimeter, which may operate in continuous wave or pulsed modes; the range gate of the latter being variable between 1 and 8 mm. The advantage of the Autosector over earlier duplex scanners is its facility for on-line analysis of flow waveforms, enabling instantaneous display of the mean, mode or peak frequency envelope and computing of the blood flow volume. In earlier, less sophisticated machines such information required that flow waveforms be stored for separate analysis at a later time. The rapid access to flow data, as provided by the on-line system, enables the hæmodynamic effects of luminal irregularities, detected by the real-time ultrasound, to be appreciated immediately, thus providing a system where image and flow data are truly complementary.

The principles of blood flow measurement using duplex ultrasound have been discussed in Chapter Two. The technique of flow measurement using the Technicare scanner will briefly be discussed below. Technical data concerning the scanner are set out in Appendix III.

Method of blood flow measurement

1. An image of the blood vessel or bypass graft under examination is obtained using the real-time imaging mode. When a suitable clearly defined longitudinal view of the vessel has been obtained, showing its maximal diameter over as great a segment of its length as possible, the image is frozen and the appropriate part of it magnified for greater clarity.

2. A point along the vessel suitable for the measurement of blood flow is chosen, and the luminal diameter at this point is measured using the electronic calipers. The + shaped cursors are positioned at the periphery of the lumen directly opposite one another. The blood

vessel diameter thus measured appears upon the screen and is stored in the computer.

3. If the vessel is irregular, or if there is doubt that the lumen is circular, then a cross-sectional view of the vessel may be obtained by rotating the transducer through 90° to provide a transverse sectional image. If the lumen is found not to be circular in cross-section, then the area may be measured by circumscribing the lumen using a dot cursor, the movement of which is effected by the use of a sensitive joy-stick control.

4. The pulsed Doppler mode is then selected, and positioned, using real-time imaging, so that the sample volume, the extent of which is indicated by the dot-markers on the beam direction indicator, embraces the whole cross-section of the blood vessel. The 8 mm range gate is that generally employed. The angle subtended by the Doppler beam with the blood vessel is measured by aligning the linear protractor cursor with the vessel lumen. The value of θ is also displayed and stored in the computer (figure 3.2).

5. When a satisfactory position has been obtained and θ measured, the pulsed Doppler mode is activated, and a continuous velocity-time Doppler shift signal, corresponding to recordings over a 10-second period, appears on the screen. This takes the form of a spectrum of frequencies indicated as a series of dots, upon which may be superimposed the mean frequency or peak frequency envelopes. As soon as a waveform series suitable for analysis is obtained, the image is frozen. The peak or mean blood flow velocity may be measured at any point along the Doppler shift waveform, by using a linear cursor. The mean flow velocity between two points of the waveform is made using + shaped cursors; these are positioned most conveniently at two points corresponding to the peak of systole flow at either end of the flow waveform in order to embrace as many cardiac cycles as possible. The volume of blood flow in units of ml/min, as calculated by the computer, appears on the screen (figure 3.3). In order to minimise error, the flow estimation is generally repeated 3 or 4 times.

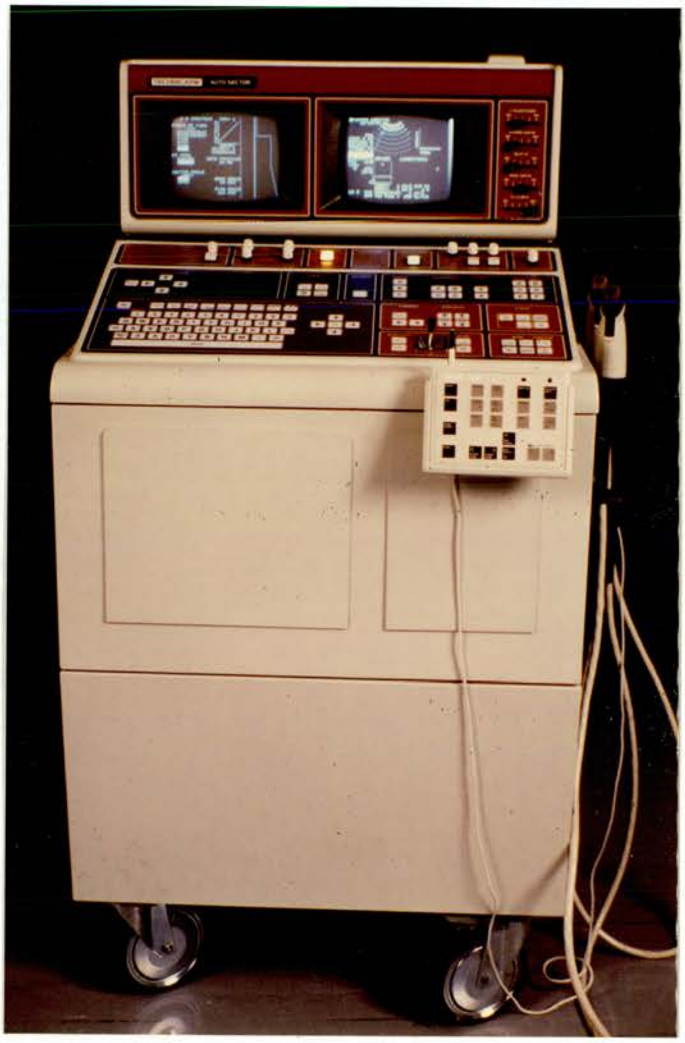


Figure 3.1: The Technicare Autosector duplex scanner

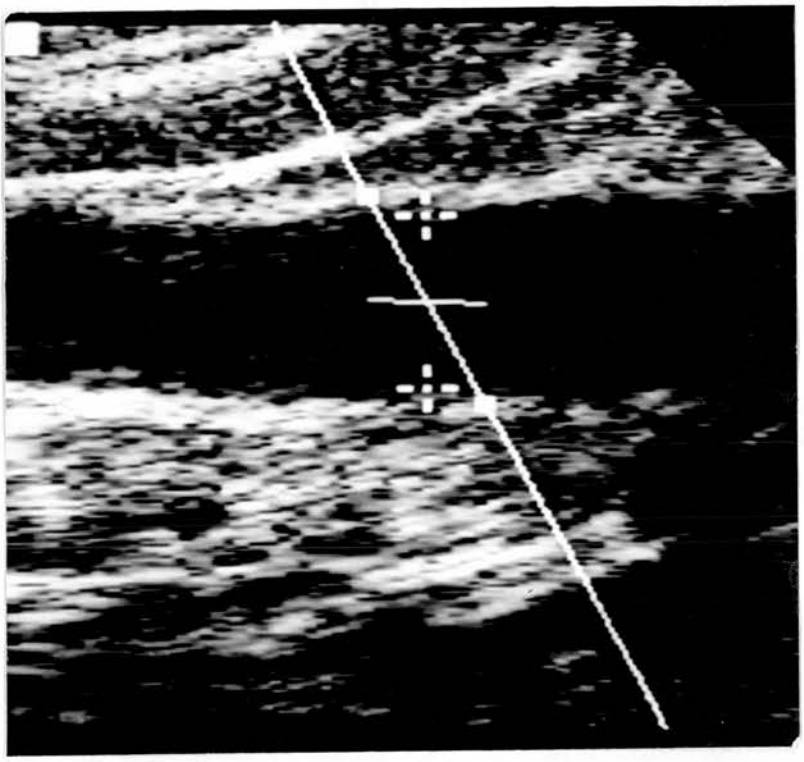


Figure 3.2: The measurement of blood vessel diameter and of the angle of incidence of the Doppler beam.
The image is a magnification of a frozen frame of the real-time B-mode scan of a saphenous vein femoropopliteal bypass. The diameter is measured by positioning the + shaped cursors opposite one another and centred on the luminal surface. The direction of the pulsed Doppler beam is indicated by the continuous line, the size and position of the sample volume by the dot markers. The angle of inclination of the Doppler beam is measured by aligning the linear cursor until it is parallel with the direction of blood flow.

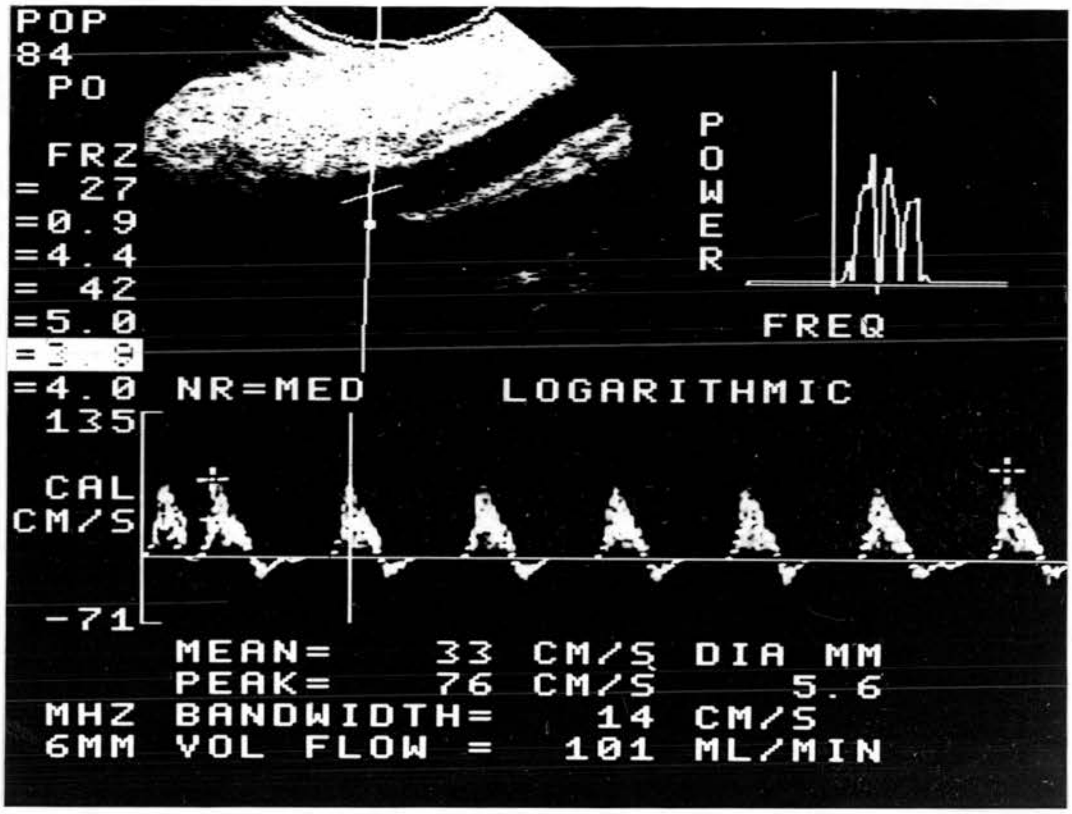


Figure 3.3: Flow recording from a femoropopliteal bypass

At the top of the screen is a frozen image from the real-time scan to show the vessel position, and the inclination and position of the Doppler beam and its sample volume. Below is a 10-second recording of the Doppler shift signal from the bypass blood flow. The wave-form is shown as a spectrum of velocities, superimposed upon which, as a dotted line, is the mean frequency (i.e. mean velocity) envelope. The vertical line is a moveable cursor, here being used to measure the mean and maximum velocity at peak systole (76 and 33 cm/sec respectively). The volume of blood flow is shown as 101 ml/min, calculated over the 6 cardiac cycles embraced by the + cursors. The diameter of the bypass at the chosen point of examination is shown as 5.6 mm (below right).

The method employed for flow measurement is open to errors, arising both from technical shortcomings and from observer error, so that the flow measurement appearing upon the screen may not, in reality, be an accurate estimation of the true blood flow. The experiments described in this chapter aim to investigate the accuracy of the technique in measuring blood flow *in vitro* compared with absolute blood flow and the effect of certain variables on the accuracy and reproducibility of the measurements.

Experiment 3.1 aimed to test the accuracy of the imaging system and the calipers in the measurement of blood vessel diameter. In experiment 3.2, measurements of the volume flow of citrated blood flowing in a flow rig were compared with absolute flow (measured by an in-circuit electromagnetic flowmeter previously calibrated against measured volume of flow using a measuring cylinder and stop-watch). Pulsatile and steady flow were both studied, and the effect of the high frequency gate filter and varying the angle of incidence observed. The reproducibility of flow measurements is tested in experiment 3.3, using flow measurements made over a period of time under constant conditions in the same common carotid artery, and using flow values recorded at different points along the length of 50 femoropopliteal bypasses.

Experiment 3.1: The accuracy of measurement of vessel diameter from the B-mode ultrasound image using electronic calipers

Methods

Fifteen tubes of various sizes were made by heat-shrinking latex tubing around drill bits of diameters from 1.0 mm to 15.0 mm, by 1.0 mm stages. The experiment was carried out in double blind fashion by two experimenters. Tubes were immersed at random into a water bath 1.5 to 5.0 cms below the surface and longitudinal images were made using the real time echo system of the Technicare scanner. A suitable image for each examination was frozen and magnified, and a measurement of diameter made using the electronic calipers, as if a flow measurement was to be made. In all, 60 measurements of diameter were made.

Results

In 55 of the 60 measurements, the true diameters differed from the measured by 0.1 mm or less. In only 2 cases did the error in the measured diameter exceed 0.5 mm. Overall, the mean error was 1.2% and the coefficient of variation 5.3%.

Flow-rig experiments

Experiment 3.2a: The measurement of continuous non-pulsatile flow

A simple flow rig was constructed with the ability to deliver blood with a continuous flow variable up to one litre per minute. A 20 cm length of 6.0mm latex tubing was connected in the circuit, and immersed 2 cms below the surface of a water bath. An electromagnetic flow meter, previously calibrated for continuous flow in the range 0 to 2000 ml/min using timed flow of blood into a measuring cylinder, was connected downstream into the circuit in series with the latex tube. The flow rig was filled with human blood with a hæmatocrit adjusted to 45%; this was used as the test fluid in all the flow experiments.

The transducer of the scanner was fixed in position just in contact with the water in order to permit estimation of blood flow within the latex tube. An angle of approach of the ultrasound beam of 55° was used. A real time image of the tube in longitudinal section was obtained, so that the maximal diameter was shown across the whole width of the image. In this way the tube was placed exactly in the plane of the ultrasound. Flow values between 10 and 1000 ml/min were randomly selected by one operator, the flow rate being adjusted to the desired rate as shown on the electromagnetic flow probe. The other operator then, in blind fashion, measured the rate of volume blood flow ultrasonically using the Technicare apparatus. For each estimation, a timed measurement of the blood passing through the rig into a measuring cylinder provided a check of the accuracy of the calibrated electromagnetic flowmeter.

The experiments were performed using continuous wave Doppler and the again an 8mm range-gated pulsed Doppler beam to estimate mean blood flow. In both cases the 200MHz high pass wall filter was employed.

Results (figs 3.4 - 3.5)

A good linear correlation was observed between actual flow and measured flow using both types of ultrasound for flow values above 50 ml/min, although ultrasonically measured values exceeded those made using the previously calibrated electromagnetic flowmeter by about 50 ml/min. For continuous wave Doppler the measured flow (Q') was related to actual flow (Q) by $Q' = 1.00Q + 51$; $r^2 = 0.998$. Using pulsed wave Doppler the correlation was $Q' = 0.96Q + 55$; $r^2 = 0.996$.

Experiment 3.2b: The effect of varying the angle of incidence of the Doppler beam on the measurement of constant flow

In order to invesigate the effect of varying the angle of incidence of the Doppler beam on the measured blood flow rate, the present study was undertaken, using the simple flow rig employed in experiment 3.2a. A constant flow rate of 200 ml/min was used throughout. The transducer of the duplex scanner was positioned so that the angle of incidence of the Doppler beam could be varied between 40° and 80°. Estimates of blood flow in the flow rig were made using angles of incidence of 43°, 46°, 48°, 50°, 53°, 56°, 58°, 60°, 63°, 66°, 68°, 70°, 75° and 80°.

Results

The measured flow rates are shown in figure 3.6. Although the flow was overestimated by about 50 ml/min, this remained a constant error provided the angle of incidence of the Doppler beam was kept below 60°. When the angle became greater than this the error rose remarkably.

Experiment 3.2c: The measurement of pulsatile flow

In order to mimic more closely the physiological pulsatile pressures and flows found in the peripheral arterial system, a more complicated hydraulic system was constructed. This model was derived from the third-order lumped parameter model derived mathematically by Goldwyn and Watt (1967). The model (see figure 3.7a) was driven by a variable peristaltic pump (P) operating at a rate of 0-200 pulses/min and delivering 0-1200 ml/min. Two constant pressure head tanks (C_1 and C_2) of variable height acted as capacitance vessels: the proximal one (C_1) corresponding to aortic compliance and the distal (C_2) to peripheral compliance. Peripheral resistance was provided by gate clamps (R_1-R_4), which could also serve as proximal and distal stenoses. An elecrical analogue of the hydraulic model is shown in figure 3.7b. Here, voltage corresponds to flow, capacitance to vessel wall compliance and inductance to the inertia of blood within the system.It was found that the system could be adjusted to provide physiological pressures, as monitored by the pressure transducer (PT), and flow values. Moreover, the flow waveforms could be altered, to provide a variable degree of reverse flow, for instance.

As in experiment 3.2a, the online electromagnetic flowmeter was calibrated by timed measurement of blood flowing through the system into a measuring cylinder. Flow measurements were made using the Technicare scanner, positioned exactly as in experiment 3.2a, using a

6.0mm internal diameter latex tube immersed in a water bath, and the system filled with citrated blood of hæmatocrit 45%. Estimations of flow were made using an angle of interrogation of 55° for both continuous wave and and pulsed Doppler with a range gate of 8mm, with and without the use of the high-pass 200MHz wall filter.

Results

Using pulsed Doppler, the flow measurements showed a linear response to the actual flow values, with a coefficient of linear correlation of $r^2 = 0.994$; $Q' = 1.07Q + 30$ (Figure 3.8). The addition of the 200 MHz gate filter improved the correlation to $r^2 = 0.996$; $Q' = 1.02Q + 26$. Using continuous-wave Doppler, there was a linear response above about 100 ml/min, but serious errors affected measurement of lower flow values (Figure 3.9). The correlation of actual and measured flow using continuous-wave Doppler was $r^2 = 0.945$; $Q' = 0.86Q + 96$. The high frequency gate filter improved this to $r^2 = 0.984$; $Q' = 0.92Q + 68$.

Tests of reproducibility

Experiment 3.3a

However accurately the results of a single measurement of flow may match the true values, a flowmeter is only reliable if its flow measurements are reproducible. Unfortunately, biological systems cannot be relied upon to produce constant rates of flow against which the accuracy of a flowmeter may be tested *in vivo*. As a compromise, it was decided to measure the resting flow under constant conditions from a constant position in the common carotid artery of a young healthy male subject on a number of occasions, on the assumption that this value would show less day to day variation than the flow in most peripheral arteries. Twenty measurements of blood flow were made from this artery on each of 5 consecutive days.

Results

The flow measurements ($n = 100$) ranged from 391 to 487 ml/min overall, with a mean of 427 ml/min and coefficient of variance (c_v) of

6.4%. The measurements (n = 20) for each of the five days were (mean: c_v) 430 ml/min: 5.4%; 423 ml/min: 4.6%; 417 ml/min: 3.6%; 437 ml/min: 5.4% and 440 ml/min: 4.7%.

Experiment 3.3b

The measurement of blood flow at different points along the length of a blood vessel should be relatively constant if performed within a short space of time under constant resting conditions. Flow measurements made at between 4 and 7 points along the length of 50 consecutive femoropopliteal bypasses were used to test the accuracy of the flowmeter in the measurement of constant flow in a blood conduit of varying calibre and distance from the transducer. The precise methods of flowmetry pertaining to femoropopliteal bypasses are described in Chapter Six. In each case, one measurement was made just distal to the proximal anastomosis and another as distal as possible within the bypass. Between 2 and 5 further measurements were made along the length of the bypass between these points.

Results

The coefficient of variation of the measured blood flow values in the 50 bypasses ranged from 1.9% to 32.7%. The mean and standard deviation of these coefficients was 12.3% ± 6.7%. In general, the flow measurement recorded from the most distal, deeply situated part of the graft tended to be lower than the remaining measurements and accounted for much of the observed variation.

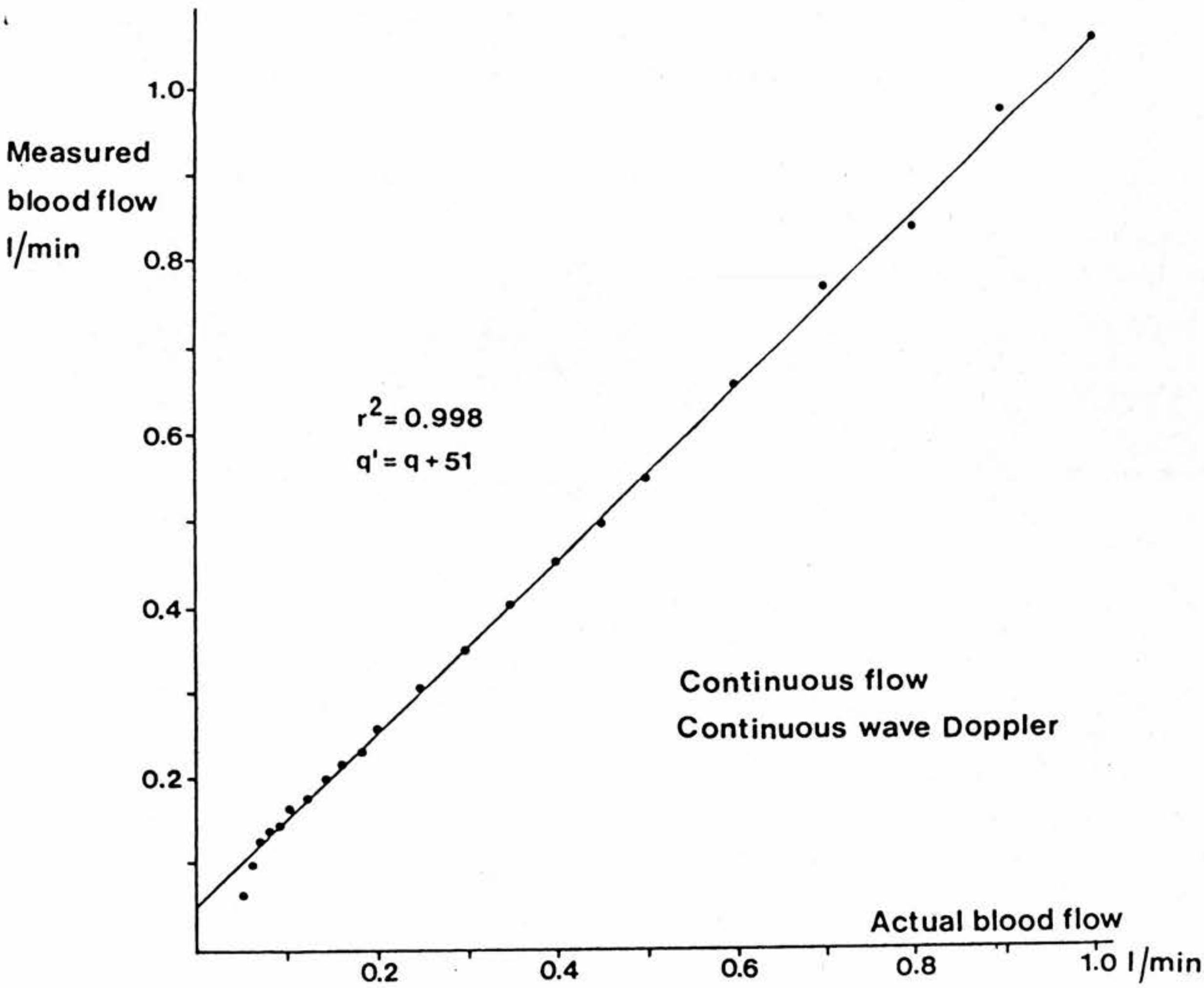


Figure 3.4: Calibration curve for continuous, non-pulsatile blood flow measured using continuous wave Doppler with the addition of a 200MHz high pass gate filter (experiment 3.2a).

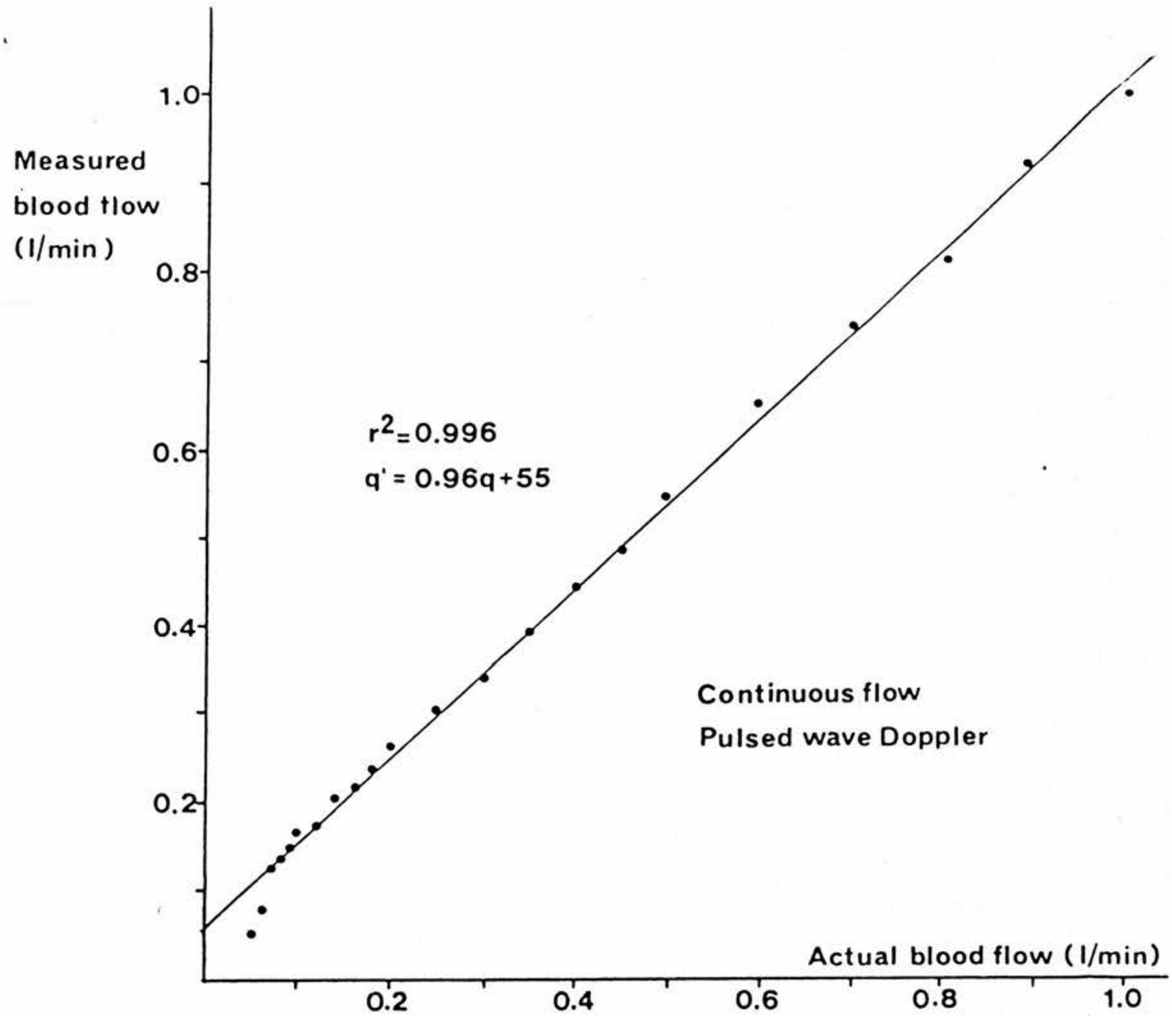


Figure 3.5: Calibration curve for continuous, non-pulsatile blood flow measured using pulsed wave range-gated Doppler with a sample volume of 8mm and the addition of a 200MHz high pass gate filter (experiment 3.2a).

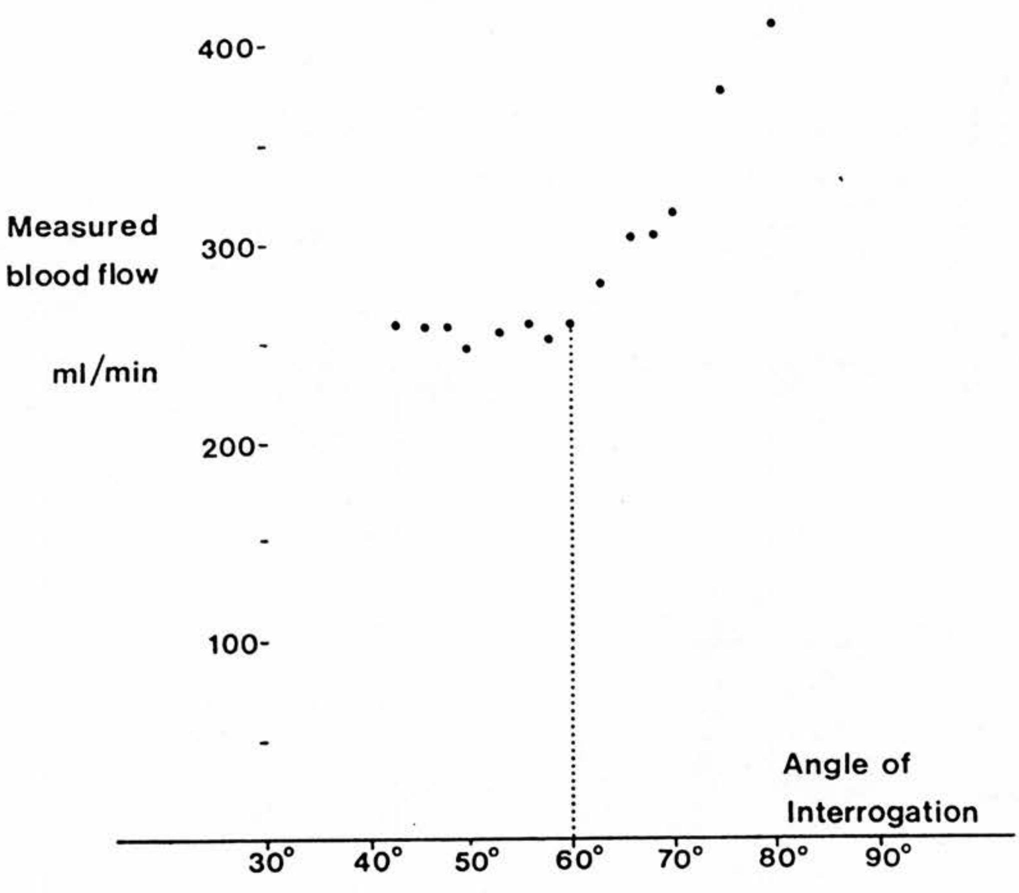


Figure 3.6: The effect of varying the angle of incidence of the pulsed Doppler beam on the measurement of steady non-pulsatile flow with a constant rate of 200 ml/min.

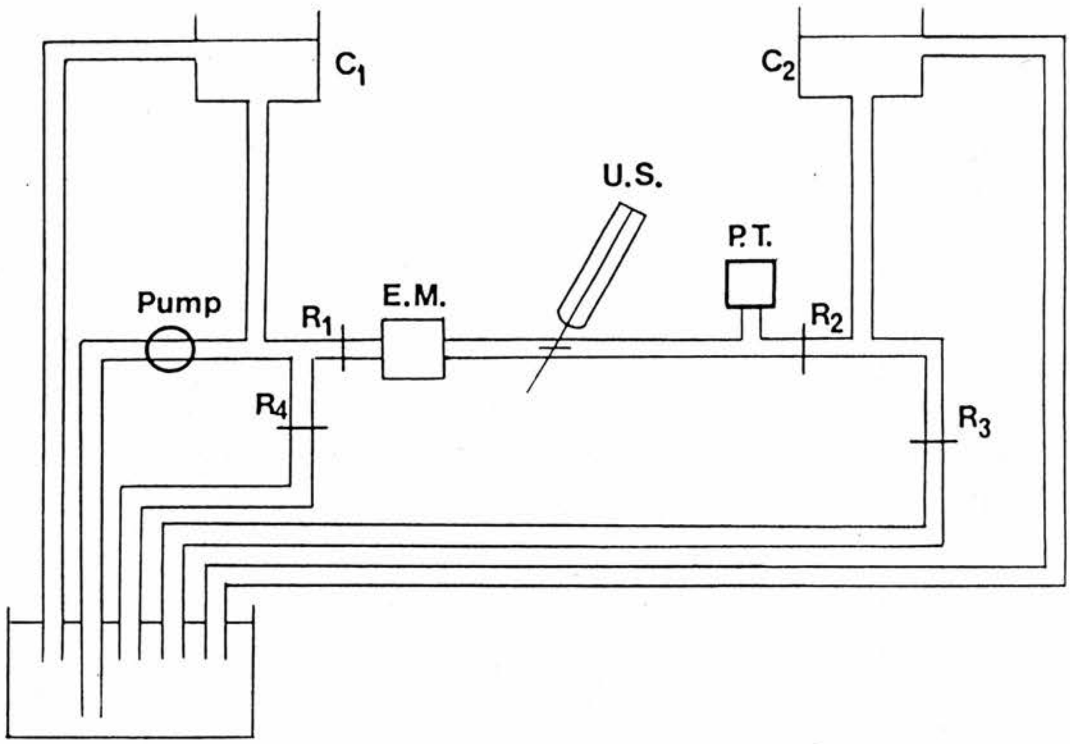


Figure 3.7a: The flow rig employed in experiment 3.2b designed to deliver pulsatile flow of citrated blood over a range of 0-500 ml/min. The apparatus is more fully explained on page 34.

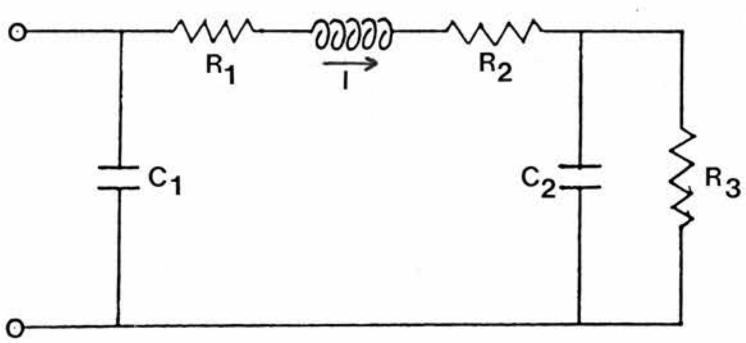


Figure 3.7b The electrical analogue of the above.

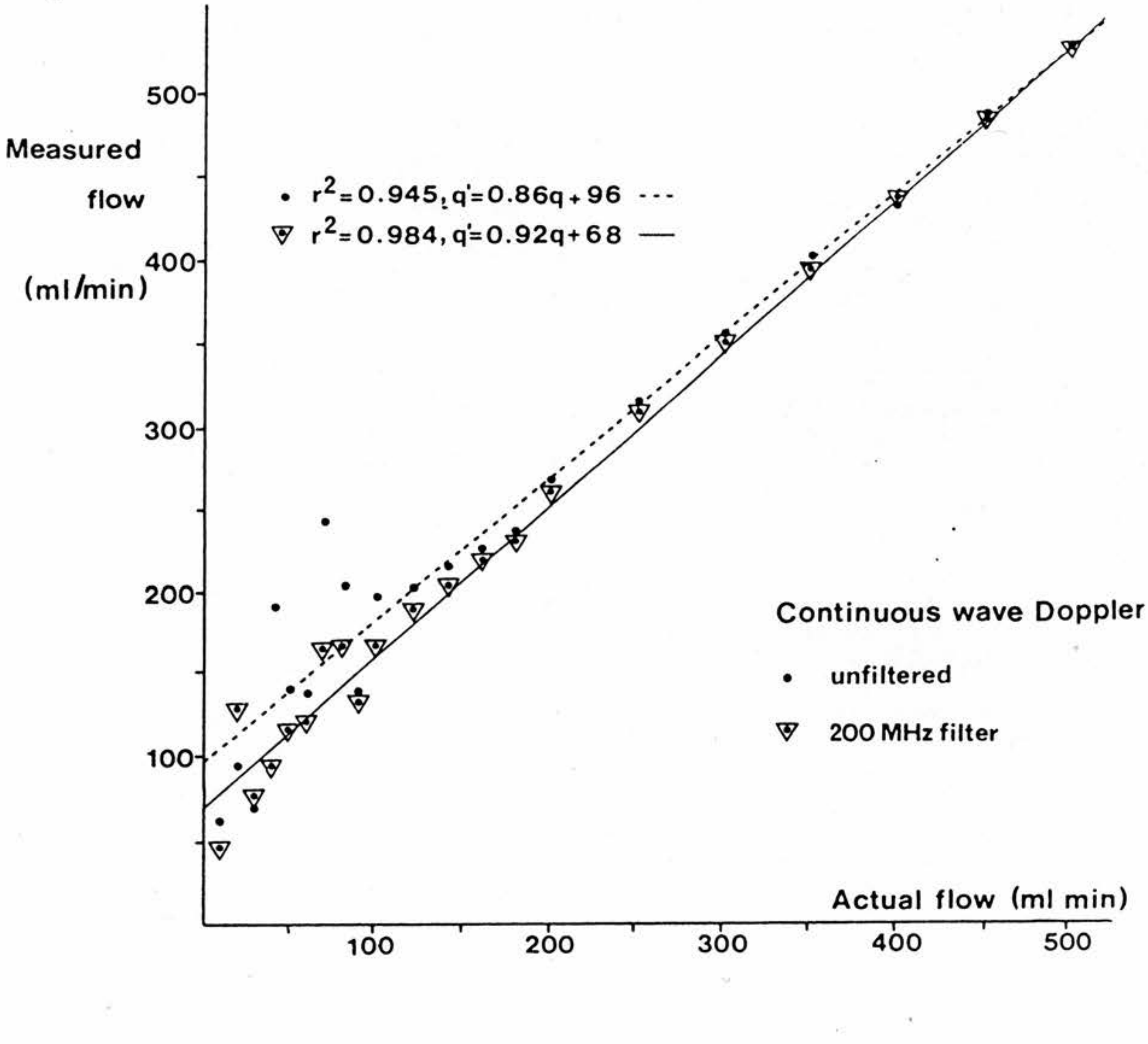


Figure 3.8: Calibration curve for the measurement of pulsatile blood flow using continuous wave Doppler, with (▼) and without (•) the use of the 200 MHz high pass gate filter (experiment 3.2c).

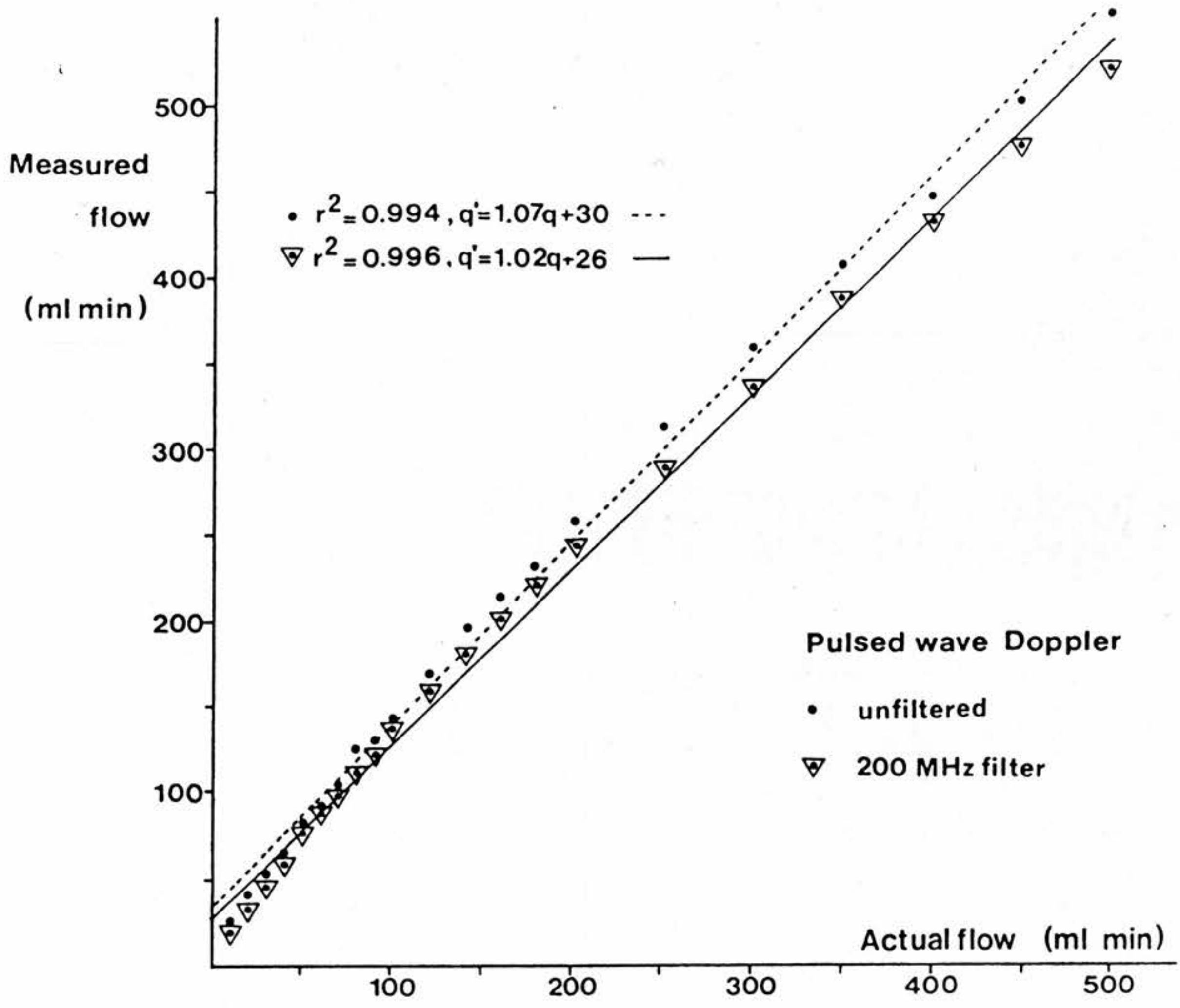


Figure 3.9: Calibration curve for the measurement of pulsatile blood flow using pulsed wave Doppler, with (▽) and without (•) the use of the 200 MHz high pass gate filter (experiment 3.2c).

Discussion

The performance of the real-time ultrasonic component of the scanner in the measurement of tube diameter is very reassuring both for flow measurement and for the usefulness of the duplex scanner to provide purely morphological data. The high resolution of the Technicare real-time system, with a wide-ranging grey scale, provided excellent images of implanted bypass grafts; this study will be described in Chapters Five and Seven. On the other hand, the very considerable error resulting from the use of angles of inclination of the Doppler beam greater than 60° emphasised very forcibly the great importance of measuring θ very carefully, and of keeping its value less than 60°. In practice, as will be described in subsequent chapters, the angle generally employed lay between 48° and 58° as it proved difficult to obtain flow signals suitable for analysis using an angle θ much less than 50°.

The flow measurements made using the Technicare scanner showed a linear response when compared with variable blood flow measured using an absolute technique; with pulsatile flow the regression line had a gradient of 1.02 with a coefficient of linear correlation of 0.996. The measurements were reproducible, with a coefficient of variance between 6% and 12%. The flow measurements shown upon the screen of the scanner differ from the true values by a constant error of about 30 ml/min. In order to allow direct comparison of the flow measured by the ultrasound system with that measured using a different technique, for example, electromagnetic flowmetry or a different Doppler-based system, a simple conversion to absolute flow units was carried out using the calibration curve of figure 3.9.

A number of authors have described *in vitro* tests for establishing the accuracy of ultrasonic flowmeters based on the principle of uniform insonification. Testing the Octoson scanner using constant steady flow in a flow-rig, Gill (1979) reported an mean flow error of 2% with a standard deviation of 14%. The same author (Gill, 1985) used pulsatile flow in a flow-rig to measure flow in an excised segment of human carotid artery using the Octoson, obtaining a regression line given by $Q' = 1.06Q + 4$ ml/min with $r = 0.99$, compared with actual flow values.

Although the gradient and regression coefficient of the calibration curve obtained by Gill are very comparable with the present study, the lower value of his ordinate intercept of only 4ml/min he found is rather less than the 26 ml/min of the present study.

In vivo studies have been used to test the accuacy of aother similar systems. Eik-Nes *et al.* (1984) compared ultrasonic flow measurements in the surgically exposed aorta of a pig with electromagnetic measurements made simultaneously. The flow rate was varied pharmacologically between 300 and 800 ml/min. The regression between the two sets of measurements was given by $Q' = 0.96Q + 8.9$ ml/min, $r = 0.91$. Avasthi *et al.* (1984) used both *in vivo* and *in vitro* methods to test an ATL duplex scanner for volume blood flow measurements. Although the results of *in vitro* studies produced a highly satisfactory regression line of $Q' = 0.98Q + 8$ ml/min, $r = 0.98$ with a standard error of ±13%, the measurements made in renal arteries in anæsthetised dogs were less satisfactory. This may have resulted from their use of a pulsed Doppler beam with too small a sample volume and the use of the mode rather than the mean frequency for the flow velocity estimation.

None of the many authors cited by Gill (1985) obtained an unsatisfactory correlation between ultrasonic measurements and absolute values. In all cases the measured and actual flow values were found to correlate, with a linear coefficient of between $r = 0.95$ and $r = 1.0$, and offsets were generally less than 16 ml/min. This is substantially less than the offset found in the present study, which was nearer 30 ml/min using pulsatile flow and pulsed Doppler. To what can the error be attributed? Gill (1985) is of the opinion that the variation in observed flow readings could be accounted for by random errors in diameter measurement and in determination of θ. The present study would certainly support the view that the accurate measurement of θ is certainly the most difficult exercise in the measurement of blood flow using the Technicare scanner, and flow measurements made using values of θ greater than 65° were certainly unreliable, no matter how much care was taken to measure θ. Other noteable sources of error were a deep-seated narrow blood conduit, such as the distal portion of a femoropopliteal bypass, and a noisy signal, either resulting from interference from blood flow in adjacent blood vessels or turbulent flow in the vessel under study. Given that the predominant source of inaccurate flow measurement is the random error in performing the measurement, this variation may be minimised by taking the average of several measurements. For the flow measurements used in subsequent studies, a minimum of four flow values was obtained.

Summary

The flow measurements made using the Technicare Autosector duplex scanner showed a good linear correlation with absolute values in both steady and pulsatile flow *in vitro*. The measured blood flow was constantly overestimated by about 30 ml/min for pulsatile blood flow using pulsed Doppler, so a calibration curve, derived by *in vitro* comparison with measured flow, was required in order to provide absolute values in subsequent experiments. The reproducibility of the technique, 6% in common carotid arteries and 12.3% in femoropopliteal bypasses, was judged to be acceptable for clinical use. Ultrasonic imaging proved very reliable in the measurement of vessel diameter, and the importance of using an angle θ less than 60° was emphasised.

Chapter Four

Lower limb studies-
normal and chronic ischæmia

Introduction

The experiments described in this chapter form a background to the blood flow measurements which, as used in the follow up of arterial reconstructions, are the basis of Chapters Six, Eight and Nine. In the first of 3 experiments described, values for resting blood volume flow, blood flow velocity and arterial diameter were established by studying 59 normal limbs of 35 subjects. The superficial position of the lower limb vessels in the groin made flow measurement relatively straightforward using the duplex scanner.

Resting measurements of blood flow (Hillestad, 1963; Strandell and Wahren, 1963; Sumner and Strandness, 1969) and ankle pressure ratio (Strandness and Bell, 1964) provide limited information, and the importance of assessment of the circulation under conditions of physiological stress been made (Strandness, 1966; Yao, 1970). The timed treadmill exercise test is widely used, but is not suitable for producing hyperæmic flow in conjunction with ultrasonic flow measurements. Reactive hyperæmia, on the other hand, allowing stress testing without moving the patient under study from the examination couch, is clearly more attractive for use with ultrasonic flowmetry. It is also suitable for the study of those with a cardiac or respiratory disorder preventing exercise testing, and for use with amputees.

<u>Experiment 4.1</u>; Measurement of volume blood flow, blood flow velocity and blood vessel diameter in the normal lower limb.

Subjects

In order to establish the physiological range of flow values at rest and after flow enhancement by exercise or reactive hyperæmia, studies were undertaken in 58 normal lower limbs of 34 subjects. A normal limb was defined as giving rise to no symptoms of arterial or venous insufficiency, with normal peripheral pulses and a resting ankle systolic pressure index of ≥ 1.0 which did not fall after exercise testing. The subjects, of whom 11 were female, ranged in age from 19 to 81 years (median = 49). None had evidence of myocardial insufficiency. In each of 10 cases, one of the limbs was excluded from study, either because it failed to meet the criteria for normality (n=2), or because it had already been the subject of a reconstruction (n=8). In the remaining 24 subjects, both limbs were studied.

Method

External Iliac/ Common Femoral Artery

Subjects were rested for 15 minutes in the thermostatically-controlled Vascular Studies Laboratory. Imaging of the lower limb arteries was carried out with the patient supine and the ultrasonic transducer placed at the inguinal crease and in the femoral triangle. It was found to be most convenient to perform flow measurements using images of and signals from the external iliac artery, rather than the common femoral artery. Not only was it generally easier to obtain a more acute angle of incidence of the ultrasonic beam, with the transducer directed rostrally and posteriorly at the inguinal crease, but this length of vessel was frequently more uniform in calibre than that distal to the inguinal ligament. Moreover, the very variable site of origin of the profunda femoris artery and of the circumflex femoral arteries often made the exact extent of the common femoral artery difficult to determine. A relatively proximally situated bifurcation of the common femoral artery occasionally resulted in turbulent signals which were difficult to analyse; a possible reason for inconsistent flow measurements might result from signals from a proximally arising superficial femoral artery in the mistaken belief that it was the common femoral.

Superficial and Profunda Femoris Arteries

The superficial femoral artery was generally easily visualised at its origin and over about 15 cms. of its course in the femoral triangle. The only difficulty commonly experienced resulted from the artery being too close to the skin for the focal distance of the transducer. A block of transsonic gel was used in such cases. The origin of the profunda artery was usually seen, the course of the artery being apparent in a few cases, and reliable values were obtained in 21 cases.

For each vessel, at least 5 measurements of diameter, peak systolic blood flow velocity and resting blood volume flow were obtained.

Results

The resting values (median and range) were as follows:

<u>Resting blood flow volume</u>		
Common femoral artery	(n=58)	347 [161-463] ml/min
Superficial femoral artery	(n=58)	198 [110-316] ml/min
Proportion of C.F.A. flow		*59% [47-70%]*
Profunda femoris artery	(n=21)	120 [53-183] ml/min
Proportion of C.F.A. flow		*38% [28-51%]*

<u>Peak systolic blood flow velocity:</u>		
Common femoral artery	(n=58)	100 [70-130] cm/sec
Superficial femoral artery	(n=58)	100 [80-110] cm/sec
Profunda femoris artery	(n=21)	80 [50-100] cm/sec

<u>Mean diameter</u>		
Common femoral artery	(n=58)	7.9 [6.6-9.1] mm.
Superficial femoral artery	(n=58)	6.4 [5.1-7.6] mm.
Profunda femoris artery	(n=21)	5.3 [4.3-6.7] mm.

There was no significant correlation between the age of the patient and the resting blood flow in the superficial or common femoral arteries.

Although the values of flow in S.F.A. and C.F.A. tended to be lower in women (169 [117-290] ml/min and 307 [245-430] ml/min respectively) than men (198 [110-316] ml/min and 351 [161-463] ml/min), these diferences were not statistically significant. In the 24 subjects in whom both limbs were studied, the ratio of the lesser common femoral blood flow to the greater was 92% [82%-97%].

A quantitative comparison of treadmill exercise and reactive hyperæmia for stress testing the lower limb

The present experiments were conducted to compare the hyperæmic response in 6 normal subjects to exercise tests and following arterial occlusion of a variety of periods of time, and to identify a reproducible means of producing a quantifiable hyperæmia for routine use in flowmetry studies. A standard treadmill exercise test of 4km/hr at 10° gradient for 2 minutes was chosen for comparison with reactive hyperæmia following 3 minutes of cuff-induced femoral artery occlusion in 18 patients with intermittent claudication.

Experiment 4.2: The effect on common femoral artery blood flow of exercise tests of varying severity and of post-occlusion hyperæmia following varying periods of circulatory arrest

Subjects and methods

Six normal, healthy volunteers (5 men, aged 21, 24, 29, 31 and 36, and a woman aged 30) were randomly subjected to a series of 5 treadmill tests of varying severity and to reactive hyperæmial tests following a range of 4 periods of arterial occlusion by a pneumatic cuff placed around the thigh and inflated to a pressure of 50 mmHg greater than the resting ankle pressure. The details of each test performed are as follows:

treadmill exercise tests:

1. one minute walking at 4 km/hr on a 10° gradient
2. two minutes walking at 4 km/hr on a 10° gradient.
3. five minutes walking at 4 km/hr on a 10° gradient.
4. five minutes walking at 6.5 km/hr on a 20° gradient.
5. ten minutes walking at 6.5 km/hr on a 20° gradient.

reactive hyperæmia following these periods of circulatory arrest:

6. one minute
7. three minutes
8. six minutes
9. ten minutes

Before each test a measurement of resting blood flow in the right common femoral artery was made. Following each test, measurements of volume blood flow were made from this artery. The first hyperæmic flow measurement was available within 10 seconds of release of the occluding cuff in the reactive hyperæmia tests; in the exercise tests the first measurement was made at about 30 seconds after the subject stepped off the treadmill. Flow measurements were repeated every 30 seconds to 4 minutes, and every minute thereafter until resting values were reached. Each test was carried out following a rest period of at least 10 minutes from the time basal flow rates had been restored after the preceding test. The 9 tests were carried out in a random order in each case.

Results

The results are shown diagramatically in figure 4.1 and listed in table 4.1.

Although 1 minute of exercise (test 1) produced a measureable hyperæmia, this was of very short duration. The hyperæmia produced by 1 minute of occlusion (test 6) was similarly very short-lived, virtually returning to normal within 1 minute. Following 2 minutes of exercise (test 2), the blood flow was still doubled after 1 minute. The hyperæmia at 1 minute and the time to recovery (about 2 minutes) in this test and after 3 minutes of occlusion (test 7) were broadly similar. After 5 minutes of exercise (test 3) the hyperæmic flow was increased and the recovery time prolonged, but further increasing the exercise load by using a steeper gradient (test 4) and a longer period of exertion (test 5) tended to prolong the recovery time rather than to increase the peak hyperæmic flow. Longer periods of occlusion (tests 8 and 9) increased flow and recovery time, but the magnitude and duration of the hyperæmia were less than following exercise of a corresponding duration. Most subjects experienced considerable discomfort after the thigh occlusion cuff had been inflated for more than about 4 minutes, but 3 minutes was well tolerated by all 6 subjects.

Table 4.1

(The flow measurements are expressed as the median [range] of $\frac{\text{resting flow}}{\text{hyperæmic flow}}$ x100% in each case.)

test	first measurement	at 1 minute	recovery time
1.	288% [171-338%]	105% [89-142%]	1'15" [1'00"-1'30"]
2.	330% [269-481%]	227% [167-411%]	2'15" [1'30"-2'30"]
3.	509% [377-481%]	400% [297-580%]	3'00" [2'30"-5'00"]
4.	496% [430-731%]	415% [340-620%]	4'30" [3'30"-8'00"]
5.	581% [474-828%]	488% [352-691%]	7'00" [5'00"-11'00"]
6.	315% [204-350%]	119% [101-143%]	1'15" [1'00"-1'30"]
7.	560% [430-690%]	240% [190-270%]	2'15" [2'00"-3'00"]
8.	648% [441-794%]	296% [237-410%]	3'30" [2'30"-6'00"]
9.	772% [588-907%]	344% [266-518%]	4'30" [3'30"-8'00"]

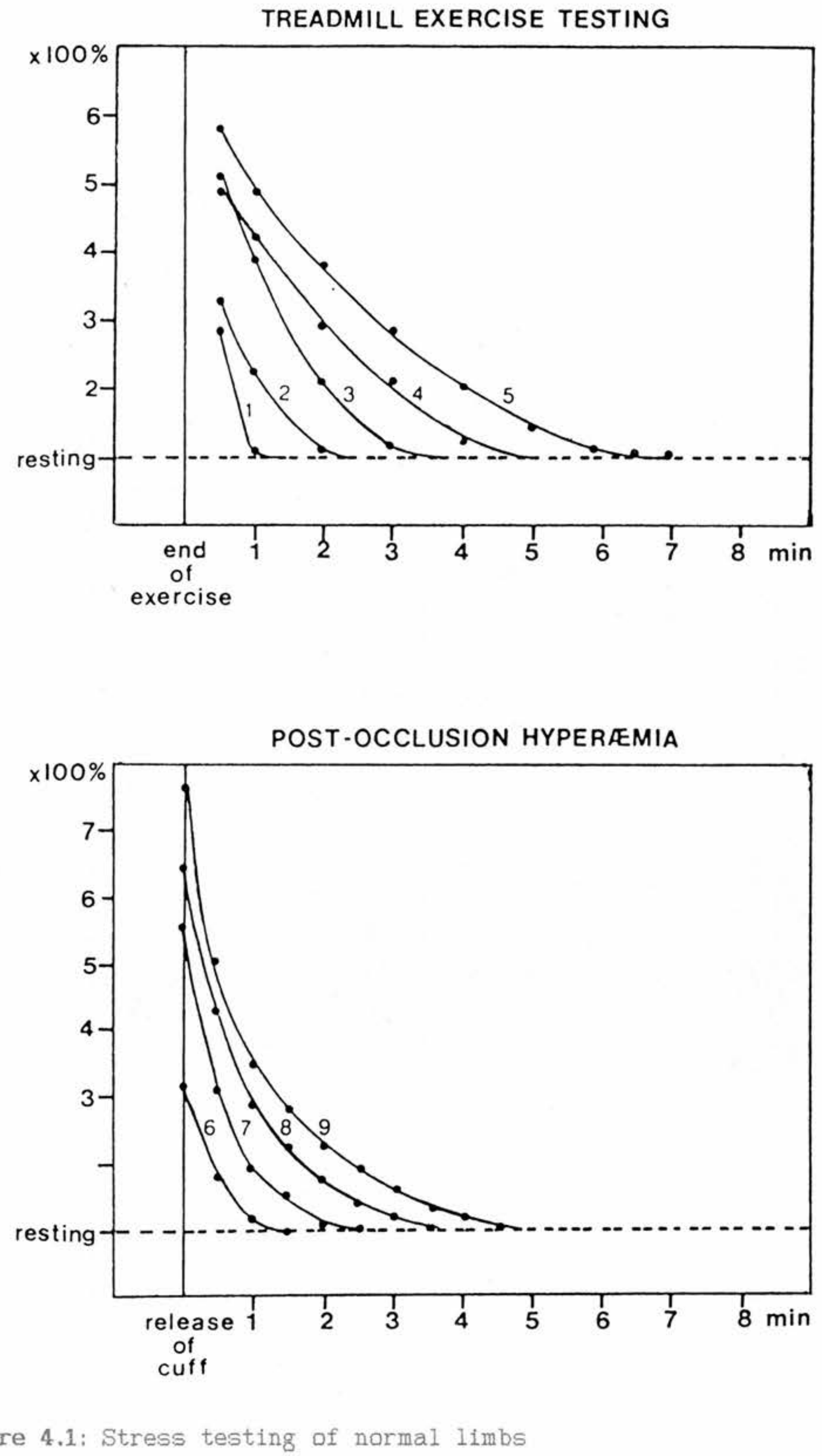


Figure 4.1: Stress testing of normal limbs

Blood flow (median values) expressed as a ratio of resting flow for the 5 treadmill exercise periods and 4 reactive hyperæmia tests described in experiment 4.2.

Experiment 4.3: Comparison of treadmill exercise testing and reactive hyperæmia for stress testing the ischæmic lower limb

Subjects

Eighteen patients who had undergone arteriographic assessment of unilateral intermittent claudication were studied. In 11 cases the claudication arose from occlusive disease of the superficial femoral artery, and in the other 7 cases iliac disease was predominant. Selection for arteriography was by routine clinical assessment and ankle pressure measurements in the outpatient clinic. Patients were studied having given informed consent. Measurements of blood flow in the symptomatic limb were made at rest and during hyperæmia induced by a two-minute exercise test (as in group 2 of experiment 4.2) and following a three-minute circulatory arrest (as in group 7 of experiment 4.2). These 2 tests produced a comparable and easily quantifiable hyperæmic response in the normal subjects and were judged likely to be well tolerated by the claudicants. Both tests were performed in all patients. In all cases the tests were performed following a rest period of at least 15 minutes. Ankle systolic pressure indices were measured at rest and following the exercise test by a second observer.

In one case, severe claudication prevented the patient from completing 2 minutes of treadmill walking. In only 2 cases did it prove possible to measure blood flow within 60 seconds of completing the treadmill test, because of the time required to get the patient repositioned on the examination couch and to obtain Doppler flow signals. In the reactive hyperæmia studies, flow measurements were all made within 15 seconds of release of the occluding cuff. As in experiment 4.2, flow measurements were repeated every 30 seconds to 5 minutes and every minute thereafter until resting flow values were reached.

Results (figure 4.2)

Resting flow values in the common femoral arteries of the 18 claudicating limbs were 198 [66-340] mls/min. These were significantly less than the normal range of values established in experiment 4.1 ($p << 0.001$, $z=5.6$, Mann Whitney). Ankle pressure ratios at rest were 0.70 [0.42-0.95], falling to 0.45 [0.21-0.65] after the two-minute exercise test.

Following release of the occlusion cuff, blood flow rose rapidly to 257% [140-570%] of the resting value and was 197% [125-391%] at one minute, returning to resting levels by 5 minutes [3'30"-11'00"]. Following exercise testing, blood flow rose, at 1 minute (in 13 patients), to 241% [130-435%] of the resting value, and was 180% [110-315%] at 2 minutes, returning to resting levels after 6 minutes [4'00"-16'00"]. The peak hyperæmia measured and time to recover resting flow levels following the two tests were not statistically different. It was considerably easier, however, to perform flow measurements after release of the occluding cuff than following exercise testing. The claudicating subjects found rapid transfer from the treadmill to the examination couch much more difficult than did the normal subjects, and accurate rapid measurement of flow in their diseased arteries was also more time-consuming.

The recovery times for the claudicants in both tests were all longer than for the normal subjects subjected to the same tests ($p<0.001$, for both stresses, Mann Whitney). The maximum flow in the reactive hyperæmia test was much less in the claudicants than in the normal subjects ($p<0.001$, Mann Whitney), but the flow values at 60 seconds after the exercise test were not significantly different, the prolonged hyperæmia of the claudicants resulting in significantly higher flow values 2 minutes after exercise ($p<0.002$). The precise point at which resting flow levels were resumed was sometimes difficult to determine; moreover, in some cases, this was very time-consuming. For this reason it was decided to use the more easily measured peak flow as a standard hyperæmic index rather than recovery time.

In the 7 patients with iliac artery disease, the peak flow during reactive hyperæmia (192% [140-262%]) was signicantly prolonged compared with the 11 with superficial femoral artery disease (274% [167-370%]) ($p<0.02$, $U=11$, Mann Whitney), and the recovery time was significantly prolonged (7 mins [5'0"-11'0"] versus 5 mins [3'30"-7'0"]) ($p<0.02$, $U=10$, Mann Whitney)

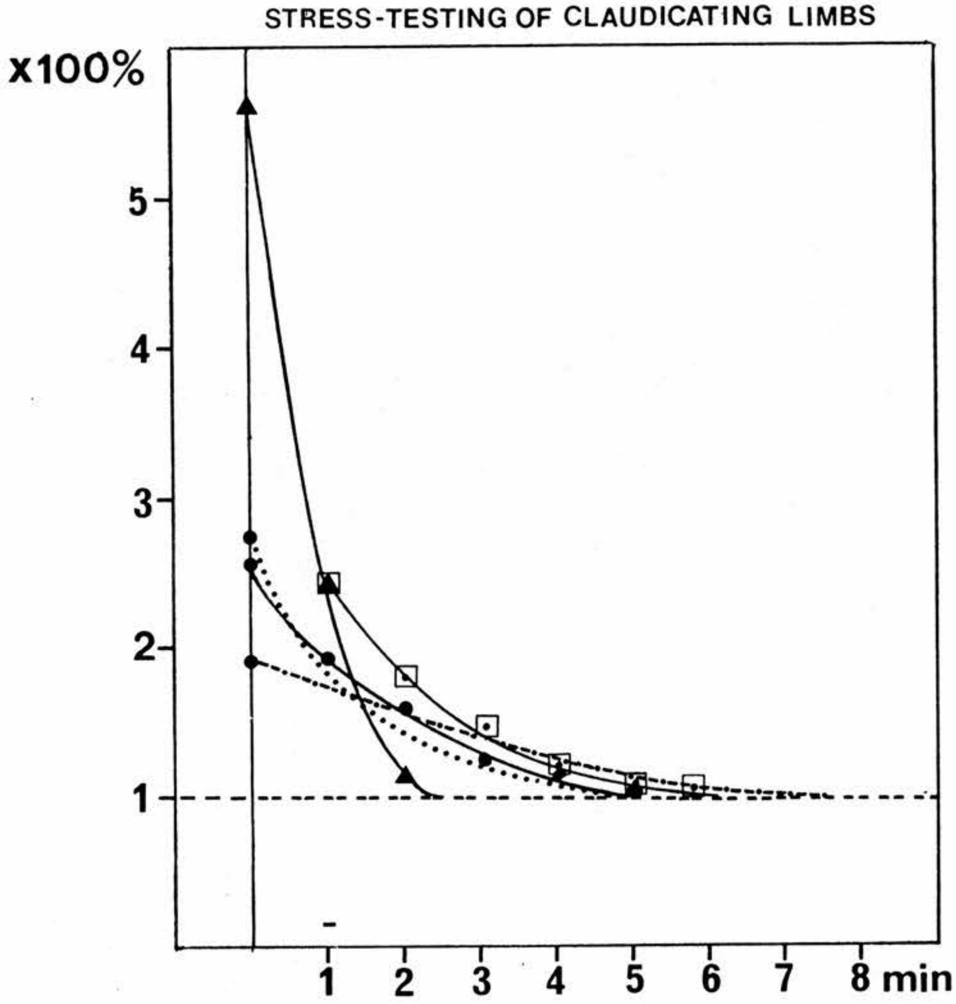


Figure 4.2: Stress testing of claudicating limbs.

Median values of blood flow, expressed as a percentage ratio of resting values, following:

- ●——● 3 minutes of cuff occlusion (all patients)
- ●–·–·● 3 minutes of cuff occlusion (iliac disease)
- ●·····● 3 minutes of cuff occlusion (S.F.A. disease)
- ⊡——⊡ 2 minutes of exercise
- ▲——▲ 3 minutes of exercise (normal control for comparison; results of experiment 4.2; figure 4.1).

Discussion

The ranges of normal lower limb blood flow as measured in this study resemble, both at rest and as enhanced by exercise and reactive hyperæmia, values obtained by other workers using various techniques (tables 4.2a and b). The peak hyperæmic blood flow and the time taken to recover resting values increased proportionately with graduated exercise testing and following lenghtening periods of cuff occlusion.

The importance of assessing the lower limb circulation under conditions of hyperæmic stress, in order to unmask any latent insufficiency of blood flow, has long been recognised. The purpose of the present study was to identify a standardised means of producing quantifiable hyperæmia which could be applied routinely to patients undergoing lower limb ultrasonic blood flow studies. Treadmill exercise for a prescribed period is currently the commonest method of stress testing the lower limb, in conjunction with ankle pressure studies. However, the time taken to move the patient from the treadmill to the examination couch, and then to set up the flowmetry equipment, makes treadmill testing less attractive for use in conjunction with ultrasonic flowmetry than a test, such as cuff-induced reactive hyperæmia, which may be performed without moving the patient from the couch. Although the longer periods of exercise testing, as investigated in experiment 4.2, produced prolonged periods of hyperæmia which certainly lasted long enough to enable flow measurements to be made, these tests were not well tolerated.

The specific advantage of reactive hyperæmia is that blood flow measurements can be made almost from the moment of release of the occluding cuff. Peak hyperæmia after 3 minutes of occlusion in normal subjects produced about 3 times the resting flow; the hyperæmic response to this test closely resembled that induced by 2 minutes of exercise. The hyperæmia following 1 minute of occlusion was found to be of too short a duration for routine use; the longer periods of occlusion than 3 minutes were not well tolerated and produced relatively small increases in peak hyperæmic flow.

Several authors have set out to compare treadmill exercise and reactive hyperæmia for stress testing lower limb circulation. In most cases the comparison was made using Doppler ankle pressures or ankle pressure indices. Ankle pressure changes following exercise testing and during reactive hyperæmia both correlated with the site and extent of occlusive arterial disease (Lewis *et al*, 1972; Johnson, 1975; Van de Water *et al*, 1980), although the time taken to return to resting values was rather shorter with hyperæmia (Hummel *et al*, 1978). Unfortunately, in most of these studies, treadmill testing was carried out until claudication was produced, rather than for a prescribed timed work load.

A possible disadvantage of assessing limb circulation using ankle pressure changes during reactive hyperæmia relates to the response in the normal lower limb. Exercise testing produces little change or, more commonly, a slight rise in the ankle pressure ratio, whereas the normal response in hyperæmia is a slight fall, in ankle pressure ratio, of the order of 15 to 20% (Johnson, 1975; Baker D., 1978). As demonstrated in the present study, this problem does not affect reactive hyperæmia blood flow measurements, which rise significantly higher in normal than claudicating subjects.

The finding that resting blood flow in the claudicating patients was significantly less than normal is contrary to the view that resting blood flow is not generally reduced in patients with intermittent claudication (Pentecost, 1964; Folse, 1964; Sumner and Strandness, 1969). In those with proximal or combined arterial disease hyperæmic flow measurements showed a significantly worse response. Not only was the peak flow reduced but the recovery time was significanly prolonged. Both Sumner and Strandness (1969), using plethysmography, and Lewis *et al* (1972), using indicator clearance, demonstrated a similar prolonging of the recovery period proportionately with the extent of arterial disease. Although the recovery period has sometimes been chosen as the index most appropriate for quantification of the hæmodynamic effects of arterial disease, in the present study it was sometimes found difficult to determine the precise point of return to resting values, Even when this could be determined precisely, several estimates of flow were necessary. The peak flow during reactive hyperæmia, on the other hand, constitutes a valuable index which is easily determined, requiring only one, or at most two, post-occlusion measurements of blood flow.

Summary

Normal values for resting blood flow in common, superficial and deep femoral arteries were established by studying 59 normal limbs in 35 subjects.

Hyperæmia produced by 5 treadmill exercise tests of varying severity was compared with that following timed periods of circulatory arrest in the lower limbs of 6 healthy young subjects.

The hyperæmic response to 2 minutes of exercise and 3 minutes of circulatory occlusion were similar. Both tests were applied to 18 patients with intermittent claudication and the resulting hyperæmic resonses measured and compared. Both forms of stress testing produced a comparable hyperæmia, which was less than in normal subjects, and recovery took much longer.

Peak hyperæmic flow, which always occured within the first few seconds of release of the occluding cuff, was chosen as a standard index of hyperæmic function, being more easily determined than the time to return to resting flow levels.

Table 4.2a

Resting blood flow in the common femoral artery

using indicator dilution		
Agrifoglio *et al*, 1961	635 [450-886] ml/min	n=12
Pentecost *et al*, 1964	440 [334-605] ml/min	n= 6
Folse, 1965	301 [196-484] ml/min	n=48
Cobb *et al*, 1969	345 ±126 ml/min	n=19
Wahren *et al*, 1973	390 ± 20 ml/min	
using thermodilution		
Ganz *et al*, 1964	636 [384-1114] ml/min	
using electromagnetic flowmetry		
Vanttinen, 1975	239 [150-420] ml/min	n=20
	134 [80-250] ml/min (S.F.A.)	n=20
	104 [50-210] ml/min (P.F.A.)	n=20
using continuous wave Doppler ultrasound		
Reagan *et al*, 1971	376 [93-627] ml/min	n=18
present study		
Lee, 1987	347 [161-463] ml/min	n=58
	198 [110-316] ml/min	n=58
	120 [53-183] ml/min	n=21

Published values for resting flow in the normal common, superficial (S.F.A.) and deep (P.F.A.) femoral arteries compared with those of the present study.

Table 4.2b

Exercise induced hyperæmia

Pentecost	exercise produced 400% to 700% increase in flow
Cobb	quadriceps exercise produced 500% increase in flow
Wahren	graded exercise produced flow increase up to 800%
Ganz	bicycle ergometer produced flow increase up to 500%
Lee	graded exercise produced flow increase up to 600% reactive hyperæmia produced flow increase up to 800%

Published values for measured percent flow increase in lower limbs produced by various work stresses compared with the results of exercise and stress tests in the present study

Chapter Five

Morphological changes in saphenous vein femoropopliteal bypasses

Introduction

Although progressive atherosclerosis in distal vessels is probably the most important cause of late occlusion of femoropopliteal bypasses, Szilagyi *et al* (1973) showed that premature failure may result from stenoses developing within the graft. Detection of such stenoses before occlusion occurs permits treatment by surgery or transluminal angioplasty. This is more likely to be successful than graft thrombectomy or regrafting using a prosthetic bypass (Berkowitz *et al*, 1981).

Ultrasonic imaging was evaluated as a method of studying implanted grafts for luminal irregularity. The role of a duplex scanner in measuring the effect of such lesions on blood flow dynamics was assessed. In this study of 77 saphenous vein lower limb bypass grafts, ultrasonic examination was undertaken to see if luminal diameter measurements could be made throughout the bypasses, and localised variations in diameter were sought. Vein valve remnants and, in *in situ* bypasses, unligated tributaries acting as arteriovenous shunts were looked for. Follow up examinations of 58 grafts were performed to examine changes in the appearance of such lesions with time.

Patients and methods

Seventy two patients with 77 implanted saphenous vein femoropopliteal or femorotibial bypass grafts were studied using the B mode imaging facility of the Autosector scanner. It was generally possible to visualise the entire length of each bypass by moving the ultrasonic transducer down the course of the bypass. The upper anastomosis was clearly seen except:

a) During the immediate postoperative period when the surgical wound and healing tissues limited the extent of the examination.
b) In patients who had previously undergone a groin arterial reconstruction, especially where the femoropopliteal bypass took origin from a more proximal graft.
c) Where the femoral triangle was involved with dense postoperative or postradiotherapy fibrosis and scarring.

The superficial position of the femoropopliteal bypass ensured that the length of the graft, except for the most distal portion in a few cases, was clearly visible. In certain *in situ* grafts and in lean patients the bypass lay too superficially for adequate visualisation and block of ultrasound-conducting gel or a saline-containing sac was required to distance the graft under study from the ultrasound transducer and to bring it within the focal zone of the imaging system.

The deeper situation of the distal anastomoses, their variable position and the inconstant route of the most distal parts of the bypasses contributed to difficulties in visualising the popliteal region of these grafts; satisfactory views of the distal anastomosis were obtained in 60% of examinations.

Each bypass was carefully examined for areas of stenosis and dilatation, and for remnants of vein valves. Cross-sectional images were also studied in order that the presence of a circular lumen could be confirmed. A minimum of 5 measurements of diameter was taken from different points in each graft; the measurements were made from a magnified frozen image of a longitudinal section of the bypass.

Of the 77 bypasses examined, 44 were studies at leat twice and 11 at least 3 times at six-monthly intervals.

Results

The majority of vein grafts showed a minimal variation in luminal calibre resulting from the irregular shape of the saphenous vein. A dilated region within the most proximal 10 cms of *in situ* grafts corresponding with the normal venous bulb adjacent to venous valves was commonly seen (figure 5.1). In 18 of the 77 bypasses studied, a >100% variation between narrowest and widest areas was seen. Of these, 12 veins were *in situ* and the remainder reversed.

Vein valve remnants

In 11 *in situ* and 3 reversed vein grafts, vein valves were observed. In each case, a freely mobile cusp of gossamer thickness was observed projecting into the blood stream and wafting to and fro with the flowing blood (fig 5.2). In one case, a thickened and rigid cusp was observed (fig 5.3). This lesion was densely fibrous but not calcified. In no case was there enhancement or broadening of the Doppler blood velocity waveform localised to the affected region of the bypass indicating a localised flow reducing stenosis. In all 6 cases, satisfactory resting and enhanced blood flow was observed. No change was observed in the 5 examined 6 months later, and it was felt that these lesions did not present a threat to the patency of the bypasses.

Stenoses

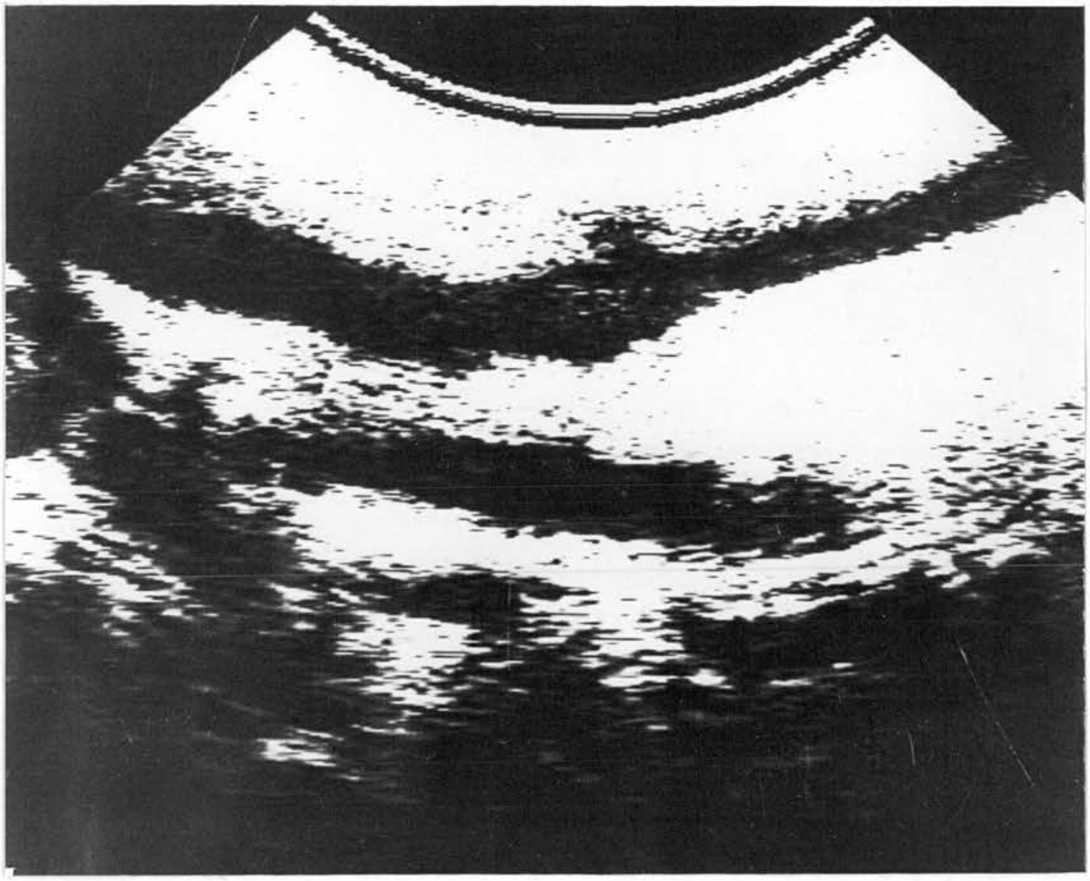
In 2 *in situ* grafts, a rounded stenosing lesion was seen projecting into the lumen in the middle third of the bypass (fig 5.4). In both cases the bypass had been implanted for more than a year, and showed no progression when examined 6 months later. The heterogenous ultrasonic density of these lesions was consistent with that seen in atheromatous plaques. It is probable that these lesions had arisen at the site of vein valve remnants, but whether by embolism or local aggregation is uncertain.

Arterio-venous fistulæ

Arterio-venous fistulæ, resulting from failure to ligate venous tributaries in *in situ* veins, were demonstrated in 3 such bypasses. In one of these the patent fistula was clearly imaged using the B mode ultrasound. In all 3 the fistula was most accurately located by detecting differential flow values in the bypass proximal and distal to it.

Graft kinking

Several of the bypasses which crossed the knee joint were visualised with the knee flexed and extended. In several cases, flexion of the knee produced a deformity of the graft with apparent narrowing of the lumen. This phenomenon was also observed in prosthetic grafts crossing joints, as will be discussed in Chapter Seven. In one case, flexion of the knee reduced resting flow in a femoropopliteal bypass by over 50%. Graft kinking at joints has been incriminated as a cause of sudden thrombotic occlusion; this will be discussed in Chapter Six.



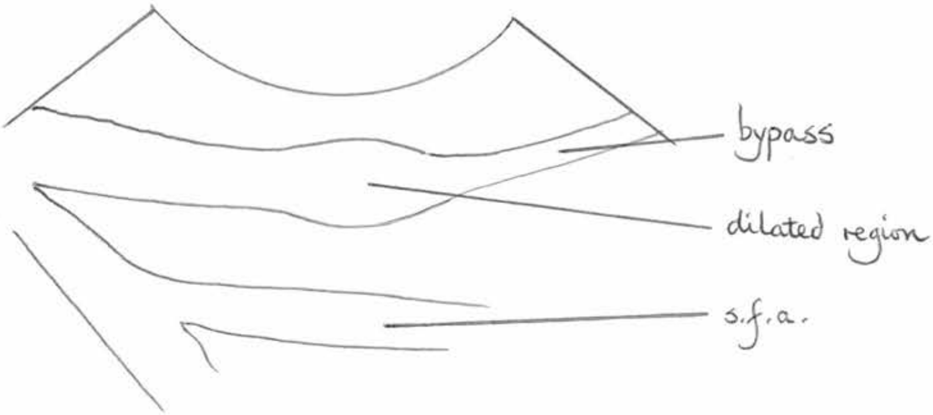


Figure 5.1: A localised area of dilatation seen within the proximal few centimetres of an *in situ* vein graft. It is presumed that this represents a venous bulb corrseponding with an area of vein valve disruption.

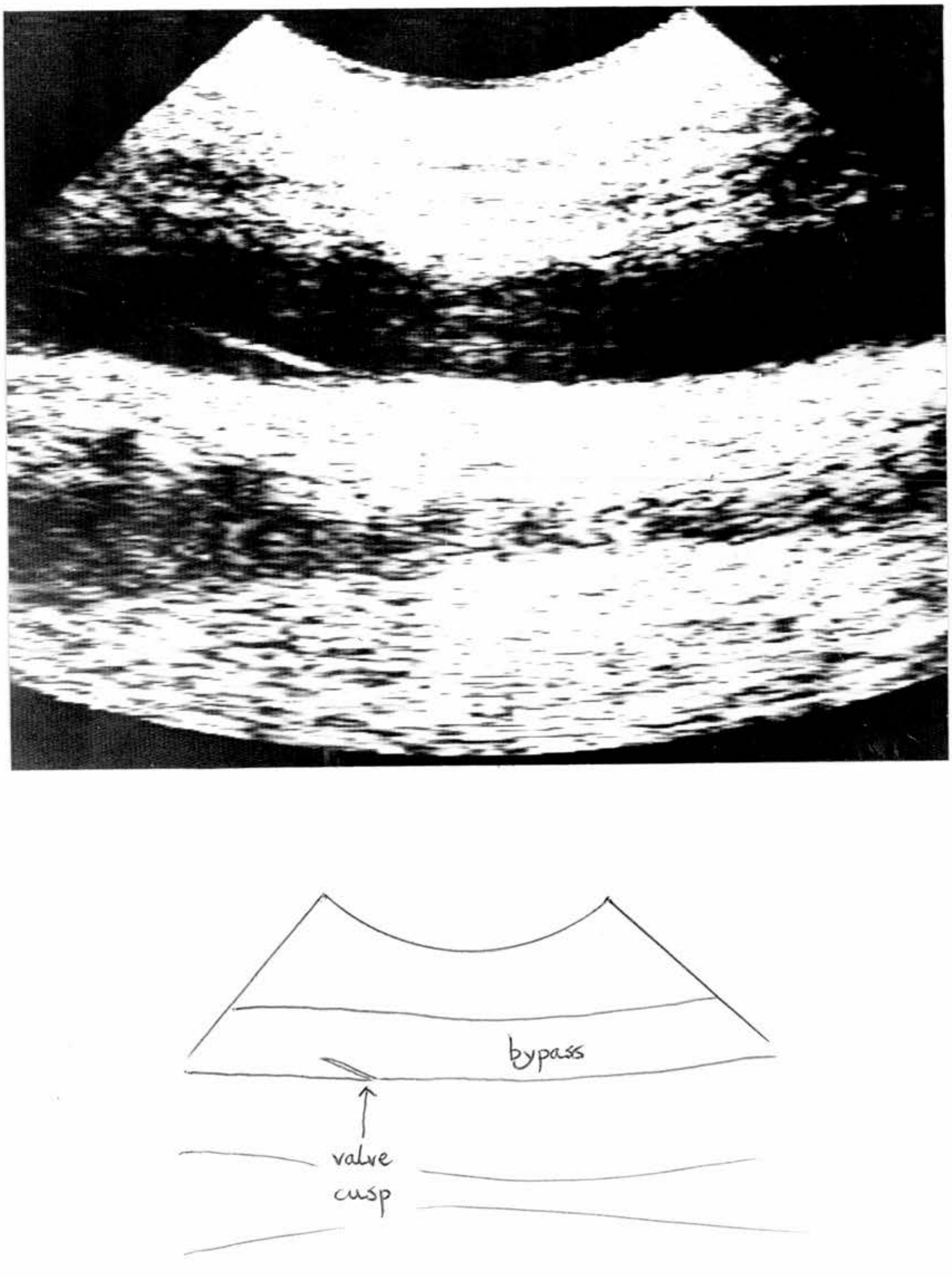
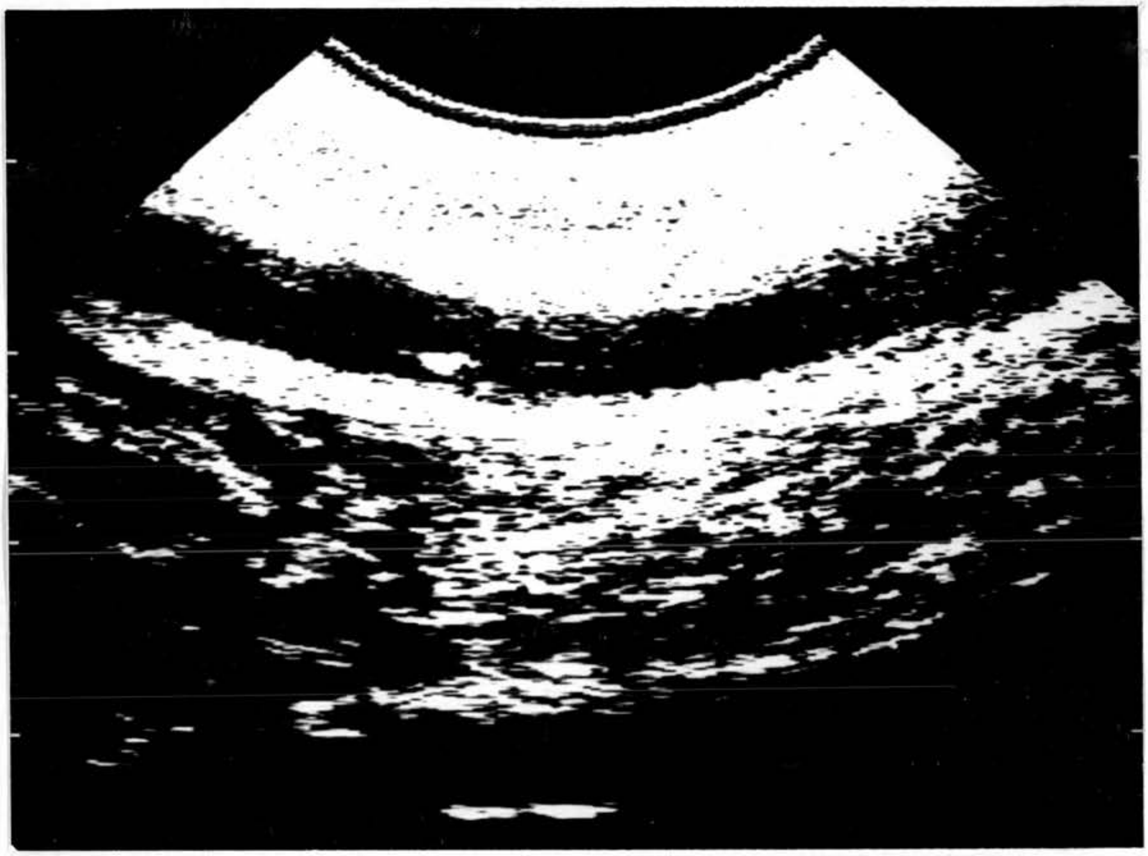


Figure 5.2: A freely mobile valve cusp projecting into the lumen of an *in situ* saphenous vein femoropopliteal bypass.



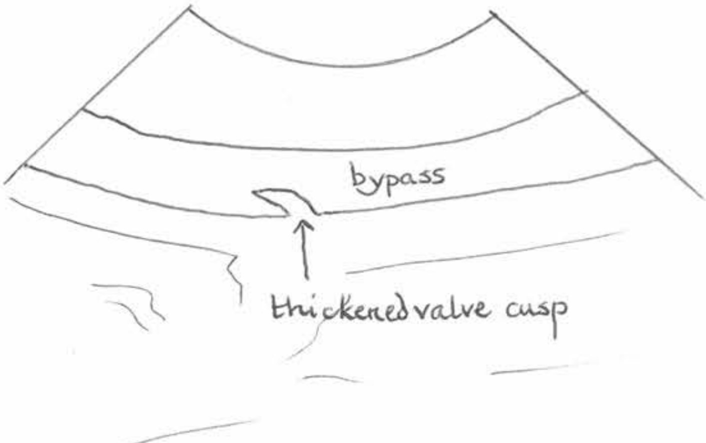
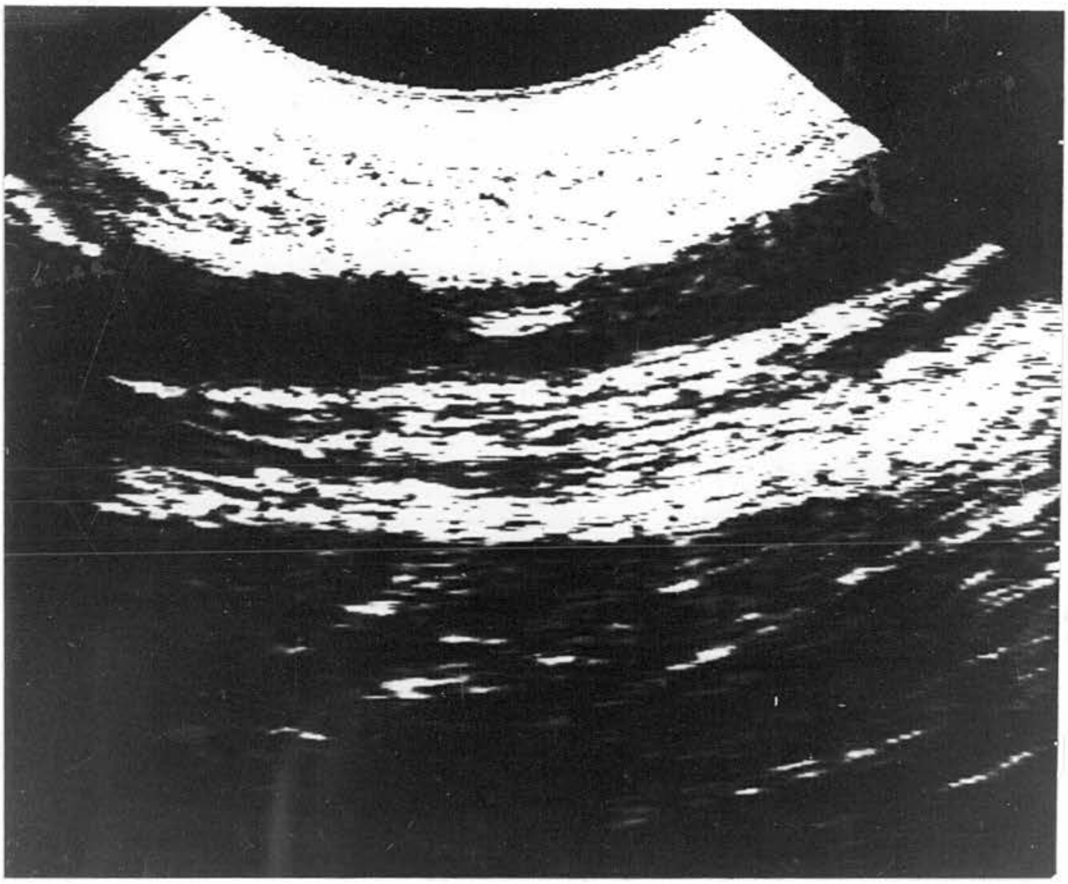


Figure 5.3: A rigid, thickened valve cusp partially occluding the lumen of an *in situ* saphenous vein femoropopliteal bypass. The absence of an acoustic shadow makes it likely that the lesion was not calcified.



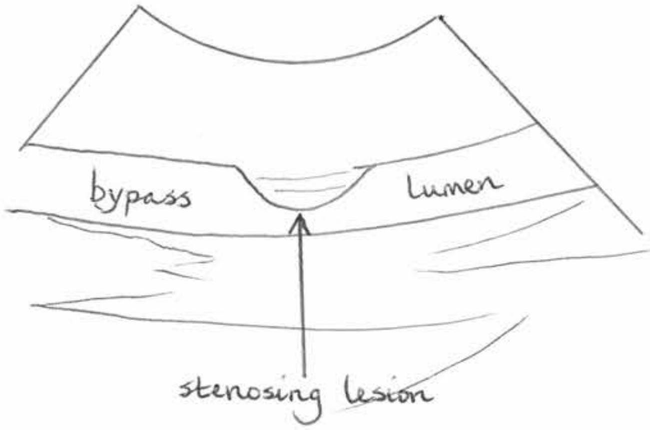


Figure 5.4: A localised, rounded lesion causing stenosis of an *in situ* saphenous vein femoropopliteal bypass.

Discussion

The real-time B-mode system used in the present study provided an efficient means of identifying mural irregularities in autogenous femoropopliteal grafts. The purpose of following arterial reconstructions using a technique such as this is to select those bypasses with lesions identified as pre-occlusive for further investigation or intervention.

Injudicious clamping, too snug ligation of tributaries and coarse suturing have all been implicated as causes of the excessive adventitial fibrosis which may result in luminal narrowing and stenosis. Vein valves or their remnants have also been regarded as the cause of localised fibrous stenosis and bypass occlusion (Breslau and Deweese, 1965; McNamara *et al*, 1967; Downs and Morrow, 1972; Szilagyi *et al*, 1973; Whitney *et al*, 1976). The incidence of vein graft stenosis ranges from 11% to 33%, with most stenoses appearing within a year of implantation (Whittlemore *et al*, 1971; Szilagyi *et al*, 1973; Whitney *et al*, 1976; Berkowitz *et al*, 1981; Sladen *et al*, 1981). In the long term study by Szilagyi *et al*, 32% of vein femoropopliteal grafts observed for 5 years developed stenosing lesions, of which 50% progressed to occlusion or required reoperation. Serial arteriography revealed that 75 % of these lesions were progressive.

Late stenosis at the site of venous valve cusps was found in 5% of reversed femoropopliteal grafts in which early postoperative arteriography was unremarkable (Szilagyi *et al*, 1973). In another large series, where the *in situ* technique had been employed using direct lysis of vein valve cusps, valve site stenosis was seen in only 3% of bypasses (Leather *et al*, 1981). Sladen *et al* (1981) classified vein valve stenoses into 3 kinds: fused valves, which generally presented early in the postoperative period; fibrosed valves, which appeared after a year or more, and multiple valve stenoses, which were seen especially in narrow calibre veins, and were of variable time of onset.

The fate of valve remnants in vein grafts has been extensively studied. Thickened and fixed valve cusps were identified by Whitney *et* *al* (1976), using postoperative arteriography, and by Clifford *et al* (1981), using real-time ultrasonic imaging. The former authors found such lesions to be progressive and associated with turbulent distal blood flow. The mobile valve cusps seen projecting into the blood stream in the present study have also been described by McCaughan *et al* (1984), who showed that, at physiological blood flow and pressure values, the valve cusps of vein grafts do not collapse against the vessel wall, but brush across the lumen, rather like the leaflets of a congenitally bicuspid aortic valve. They found that the valves occupied 61±12% of the cross section of the lumen during diastole. In an experimental study using reversed and *in situ* vein grafts in dogs, Donovan and Lowe (1985) found that valve cusps in *in situ* grafts shrank away during the early postoperative period, but that undivided valve cusps in the reversed veins were still grossly normal 7 weeks after implantation. Although there is general agreement that valve cusps persist and may be identified in established vein grafts, the question of whether they are the site of progressive luminal narrowing is not resolved. Although Wolfe *et al* (1987), using serial digital subtraction angiography (D.S.A.), identified no valve-related stenoses, this thesis would certainly support the observation that a small proportion of cusp remnants do become thickened and immobile, although those identified seemed to produce no measureable effect on graft function. In respect of D.S.A., any changes in the appearances of vein grafts with time may be due to a change in the image rather than a change in the vessel wall, since current D.S.A. images are generally less good than conventional contrast arteriography

In their large series of femoropopliteal grafts, Szilagyi *et al* (1973) found intimal hyperplasia and atheromatous changes in 4 each out of 21 bypasses examined at autopsy. They reported an incidence of 21% of atheromatous plaques in their vein grafts examined arteriographically, with a mean time of onset of 45 months. Both fibrointimal hyperplasia and atheromatous changes would appear to be much more prevalent in saphenous vein aortocoronary grafts than in bypasses to the extremity (Szilagyi *et al*, 1973). Vein graft mural ischæmia, endothelial injury, exposure to arterial blood pressure, over distention prior to insertion and platelet mitogenic factors are all variously implicated in the ætiology of these lesions.

In two *in situ* bypasses in the present study discrete lesions were seen causing a greater than 50% narrowing of the graft lumen (fig 5.4). Although resembling atheromatous plaques, one can only speculate as to the exact histological nature of these lesions. No other lesions causing a 50% narrowing of the lumen were identified in any vein grafts; indeed, most narrowed regions were observed in those grafts which showed a diffuse irregularity of the lumen. Diffuse luminal dilatation, as identified in many of the *in situ* bypasses in the present study, has been described in approximately 50% of aortorenal saphenous vein grafts (Stanley *et al*, 1978). True aneurysms have been described in about 5% of aortorenal (Stanley *et al*, 1978) and femoropopliteal (Szigalyi *et al*, 1973) vein grafts, although none was seen in the present study.

Correction of localised stenosing lesions in arterial bypasses, by reoperation or by transluminal angioplasty, yields much better results than attempts to salvage a thrombosed graft (Szilagyi *et al*, 1973; Clowes *et al*, 1980; Sladen *et al*, 1981; Berkowitz *et al*, 1981). Criteria have yet to be established to identify which lesions are progressive and likely to be pre-occlusive, therefore requiring further investigation. Minor wall irregularities were observed in a large proportion of grafts, and although these showed a slight variation from one examination to the next, none progressed to a functional stenosis. Larger stenoses may cause a recurrence of ischæmic symptoms or hæmodynamic changes detectable by flow measurements or serial ankle pressure studies (Taylor and Fox, 1977); the value of these parameters as predictors of bypass occlusion will be discussed in the next chapter.

The role of duplex scanning probably lies in the selection of a high-risk subgroup within the population of femoropopliteal bypasses. This subgroup might include asymptomatic stenoses which are associated with a flow disturbance. Arteriography should be considered with a view to selective correction. In the case of the 2 bypasses with an established stenosis in the present study, no progression was observed over a 6 month period between examinations. Since both these grafts showed satisfactory function clinically and on hyperæmic testing, the patients were not submitted to arteriography, but were followed-up non-invasively; to date these bypasses remain patent and function normally. The difficulty is knowing at what stage to submit an asymptomatic patient, with a bypass which is apparently functioning satisfactorily, to invasive investigation and angioplsty or surgery, all of which risk making the clinical situation worse. If a stenosis in such a bypass is shown to be progressive or to become associated with a hæmodynamic abnormality, then further action is justified. It would seem that duplex scanning offers an attractive means of identifying such a high-risk situation.

Chapter Six

Flow in femoropopliteal bypasses

Introduction

Although intraoperative flow measurements have long been used as predictors of patency in femoropopliteal bypass, they have not proved effective in anticipating failure after the immediate post-operative period. Follow up of arterial bypasses generally rests on a clinical evaluation and ankle systolic pressure measurements. Ultrasonic techniques have permitted quantitative analysis of Doppler shift signals from the flowing blood, including the measurement of blood flow. Femoropopliteal bypasses are ideal for follow-up by duplex ultrasonic flowmetry because almost the entire length of each bypass can clearly be visualised using the real-time ultrasound, and flow measurements are easily made. The difficulty in obtaining flow measurements during physiological hyperæmia can be overcome by using a post-occlusion reactive hyperæmia test, as described in chapter 4. Moreover, the relatively high incidence of problems, including hæmodynamic failure and thrombotic occlusion, which affect femoropopliteal bypasses much more frequently, for example, than aortofemoral reconstructions, may justify a careful follow-up using such a technique.

With the aims of establishing the range of blood flow values corresponding with satisfactory bypass function, 85 femoropopliteal and femorotibial bypasses were studied prospectively over a 12 month period with six-monthly follow up consisting of a clinical assessment, ankle pressure incides (A.B.P.I.) and ultrasonic volume blood flow measurements both at rest and following a standard hyperæmic test.

Flow measurements were compared with symptoms, A.B.P.I., bypass diameter and arterial run-off asssessed arteriographically. Using the data obtained from prospective study, the accuracy of flow measurements in the prediction of bypass occlusion was compared with that of other non-invasive parameters.

Patients and Methods

Patients with femoropopliteal and femorotibial bypasses were recruited in two ways. First, 41 patients who were thought to have a patent femoropopliteal or femorotibial bypass were invited to attend for examination. Of the 33 patients who attended, 3 were found to have occluded bypasses and were excluded from the study. Fifty patients with 55 newly inserted bypasses were recruited prospectively during the following year. Each was studied at between 1 and 6 weeks postoperatively. In all, 80 patients with 85 bypasses were studied; the patients, of whom 64 (80%) were men, were aged 64 [46-85] years (median [range]) at recruitment to the study.

Patients were questioned about symptoms of arterial disease, including myocardial ischæmia and stroke, smoking habits and drug history. Clinical examination consisted of palpation of peripheral pulses and of bypass pulsation, and an inspection of the distal lower extremities for ischæmic changes.

Investigations included resting and stress testing with the Technicare duplex scanner and ankle brachial pressure indices (A.B.P.I.). The full length of each bypass was imaged using the real-time B mode scanner, and blood flow volume was measured at a minimum of 4 points along the length of the bypass. Resting measurements were complemented by measurement of the peak blood flow during a reactive hyperæmic test. A pneumatic tourniquet placed below the knee beyond the end of the bypass graft was rapidly inflated for 3 minutes to a pressure of 50mm Hg greater than the systolic blood pressure. Immediately after release of the cuff, an estimate of blood flow was made, and repeated at 30 seconds; the larger value was recorded as the peak hyperæmic flow.

Resting ankle systolic blood pressures were recorded for each lower limb and expressed as a ratio of the brachial systolic pressures. The ankle brachial pressure index (A.B.P.I.) was also measured following a treadmill exercise test at 4km/hr on a 10% gradient for 2 minutes. For those patients unable to complete the treadmill test, a corridor walk or a three-minute hyperæmic test was substituted instead. In addition, on the first visit of each patient, a 10MHz multidirectional continuous wave ultrasonic flow probe was used to provide Doppler shift flow signals from the femoral artery in the groin and the dorsalis pedis artery or posterior tibial artery at the ankle. From these signals, a microcomputer was used to calculate pulsatility indices (P.I.)(Gosling *et al*, 1971) and the Laplace transform δ coefficient of damping (Skidmore and Woodcock, 1980).

At six-monthly intervals patients were recalled and examined as before. Those whose bypasses had occluded were again excluded. Of the 30 patent bypasses in patients studied retrospectively, 25 were studied a second time and 6 a third time. Of the 55 newly implanted bypasses, 36 were studied a second time and 5 on a third occasion. A total of 155 examinations was carried out. Eleven were studied at least three times, 48 were studied twice and 26 once only. During the 15 month study, four patients died, of whom two are thought to have had patent bypasses at the time of death, and 19 bypasses occluded or required salvage surgery.

The accuracy of flow measurements, at rest and during hyperæmia, in detecting suboptimal function in those bypasses which subsequently occluded was compared with that using clinical and non-invasive parameters.

Table 6.1

The types of femoropopliteal bypasses

	n=	*in situ* vein	reversed vein	fabric graft
established	30	8	19	3
newly implanted	55	39	10	6
total	85	47	29	9

Results

Blood flow (figure 6.1)

Blood flow (median + range) at rest was 128 [26-334] ml/min, rising by a maximum of 145% [5-647]% to 289 [27-1127] ml/min during the hyperæmic test. The first flow rates recorded in newly implanted bypasses were 135 [26-334] ml/min, and in the established group 120 [74-214] ml/min. Flow rates in 19 bypasses examined within two weeks of implantation were significantly greater than at all periods greater than two weeks ($p=0.004$, $z=2.9$, Mann Whitney).

Correlation with symptoms

The resting flow values of those patients whose femoropopliteal bypass had restored them to an asymptomatic state.were significantly greater than those with mild residual intermittent claudication (89 [60-149] ml/min) and those with unrelieved rest pain or severe claudication (35 [25-67] ml/min) ($p<0.001$, $H=28$, Kruskall Wallis test)(fig 6.1a). If peak hyperæmic flow values are considered, the differences are yet more pronounced (147 [77-352] ml/min and 48 [27-108] ml/min respectively)($p \ll 0.001$, $H=42$, Kruskall Wallis test) (fig 6.1b).

Blood flow measurements compared with other methods of non-invasive assessment

The A.B.P.I. at rest was 1.0 [0.3-1.2] and 0.9 [0.1-1.3] after stress testing. Resting A.B.P.I. showed a significant correlation with resting blood flow ($r_s=0.46$, $t=6.2$, $p \ll 0.001$, Spearman's rank correlation) (fig 6.2). Similarly, the stressed A.B.P.I. and peak hyperæmic flow correlated significantly ($r_s=0.73$, $t=12.8$, $p \ll 0.001$) (fig 6.3). There was no significant relationship between blood flow values and Laplace δ or ankle P.I., although the correlation between ankle P.I./femoral P.I. ratio was just significant ($r_s=0.29$, $t=2.6$, $p<0.02$)

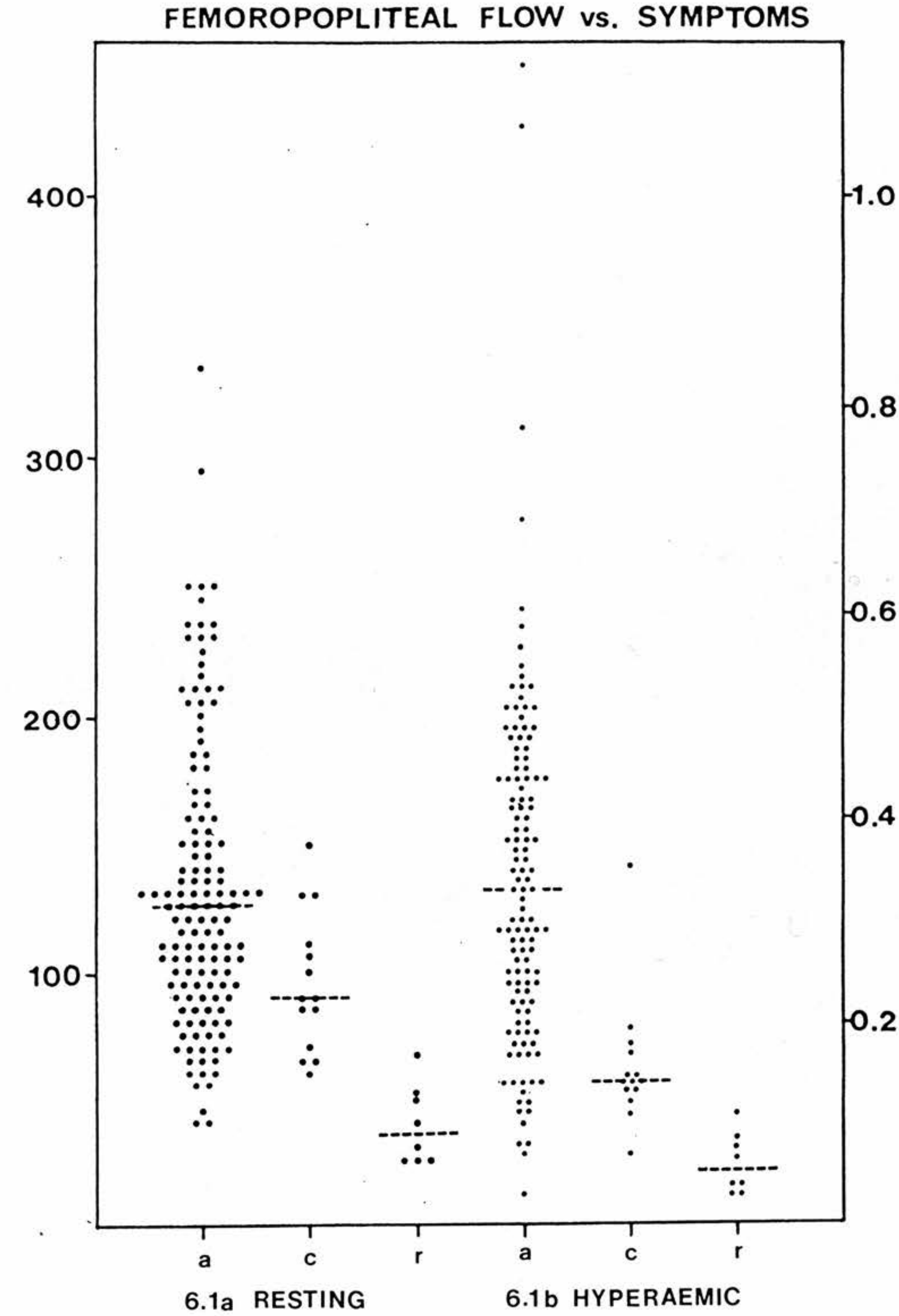


Figure 6.1: Resting (•)(figure 6.1a) and hyperæmic (•)(figure 6.1b) flow in femoropopliteal bypasses in asymptomatic limbs (a), claudicating limbs (c), and limbs which gave rise to rest pain (r). The resting flow values in ml/min are given by the left ordinate, the hyperæmic values in l/min by the right ordinate. Median values indicated by broken lines.

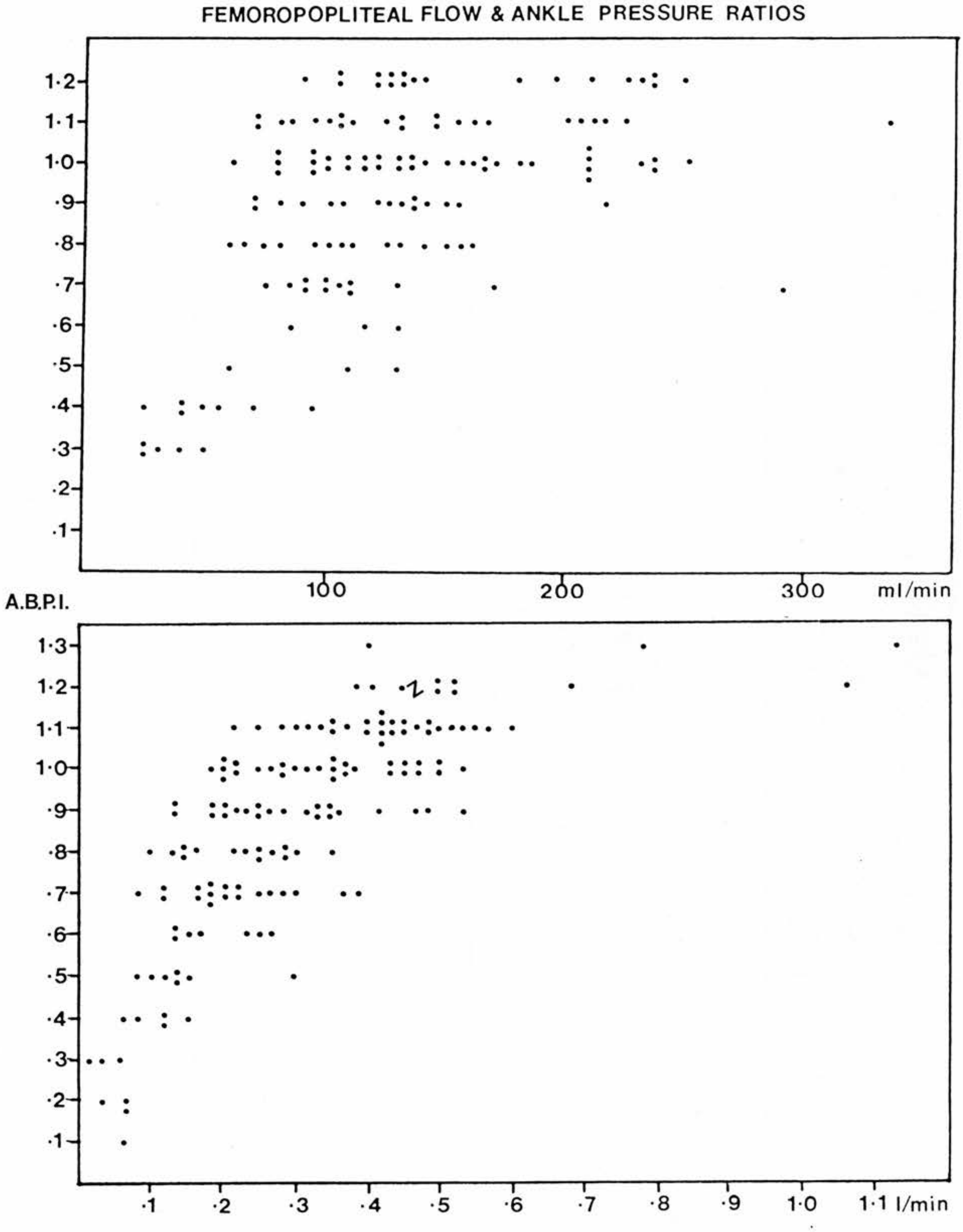


Figure 6.2 *(above)*: Resting blood flow correlated with resting ankle systolic pressure ratios. r_s=**0.46**

Figure 6.3 *(below)*: Peak hyperæmic blood flow correlated with postexercise ankle systolic pressure indices. r_s=**0.73**

Blood flow related to the arteriographic assessment of peripheral outflow

The preoperative arteriographic run-off for each group of bypasses is set out in table 6.2. Mean values of resting and hyperæmic blood flow according to graft type and run-off are in table 6.3, and in figure 6.4.

Table 6.2

	n=	3 vessels	2 vessels	1 vessel	i.p.s.
in situ vein	47	21	11	13	2
reversed vein	29	16	7	5	1
fabric graft	9	5	1	3	0
total	85	42	19	21	3

In 67 cases the lower anastomosis was to the popliteal artery, above the knee in 5 cases and below in 62. In 12 cases the tibio-peroneal trunk was used and in the remaining 5 the lower anastomosis was to a tibial vessel: in 2 each to the peroneal and anterior tibial arteries and in 1 to the posterior tibial.

Blood flow, both resting and enhanced, was significantly greater where two or three vessels provided run-off than where only one patent calf vessel or an isolated popliteal segment (i.p.s.) was present ($p \ll 0.001$, $z=3.8$, Mann Whitney) (fig 6.4). Flow values for the 21 bypasses for which only a single calf vessel provided run-off are shown in table 6.5 and depicted in figure 6.5, according to which vessel was patent. The low flow hyperæmic values seen particularly in bypasses with run-off only into an anterior tibial artery were significantly worse than those for isolated peroneal or posterior tibial run-off ($p<0.05$, $U=17$, Mann Whitney).

Blood flow, both resting and stressed, was statistically similar for the 12 grafts with a tibio-peroneal trunk run-off, to the 67 with an anastomosis to the popliteal artery ($z=0.87$, Mann Whitney). The blood flow in grafts with a single anterior tibial or peroneal vessel anastomosis was significantly worse than those which, although only one vessel provided run-off, received a more proximal anastomosis. ($p=<0.05$, $U=5.5$, Mann Whitney). This increased flow probably arose from retrograde perfusion of the proximal popliteal artery.

Table 6.3

Resting and **hyperæmic** blood flow (ml/min) (median + range) according to graft type and arterial run-off (figure 6.4)

	3 vessels	2 vessels	1 vessel	i.p.s.
in situ	142[69-234]	131[84-292]	93[26-217]	66[30-101]
vein	**340[148-554]**	**356[171-483]**	**157[32-398]**	**107[37-176]**
reversed	128[49-204]	116[81-144]	84[69-98]	100
vein	**282[92-1099]**	**303[266-735]**	**150[124-222]**	**142**
all veins	135[49-234]	122[81-292]	90[26-217]	100[30-101]
	340[148-1099]	**351[171-735]**	**154[32-398]**	**142[37-176]**
fabric	161[136-204]	92	114[40-144]	-
	450[286-502]	**130**	**190[70-371]**	-
all	143[49-234]	116[81-292]	93[26-217]	100[30-101]
bypasses	**344[92-1099]**	**303[136-735]**	**174[32-398]**	**142[37-176]**

Table 6.4

Blood flow (ml/min) (median + range) in bypasses with a single calf vessel run-off (figure 6.5)

	n=	resting flow	hyperæmic flow
Anterior Tibial	6	57 [25-130]	93 [27-207]
Posterior Tibial	5	107 [77-152]	230 [190-354]
Peroneal	10	91 [40-208]	187 [61-390]

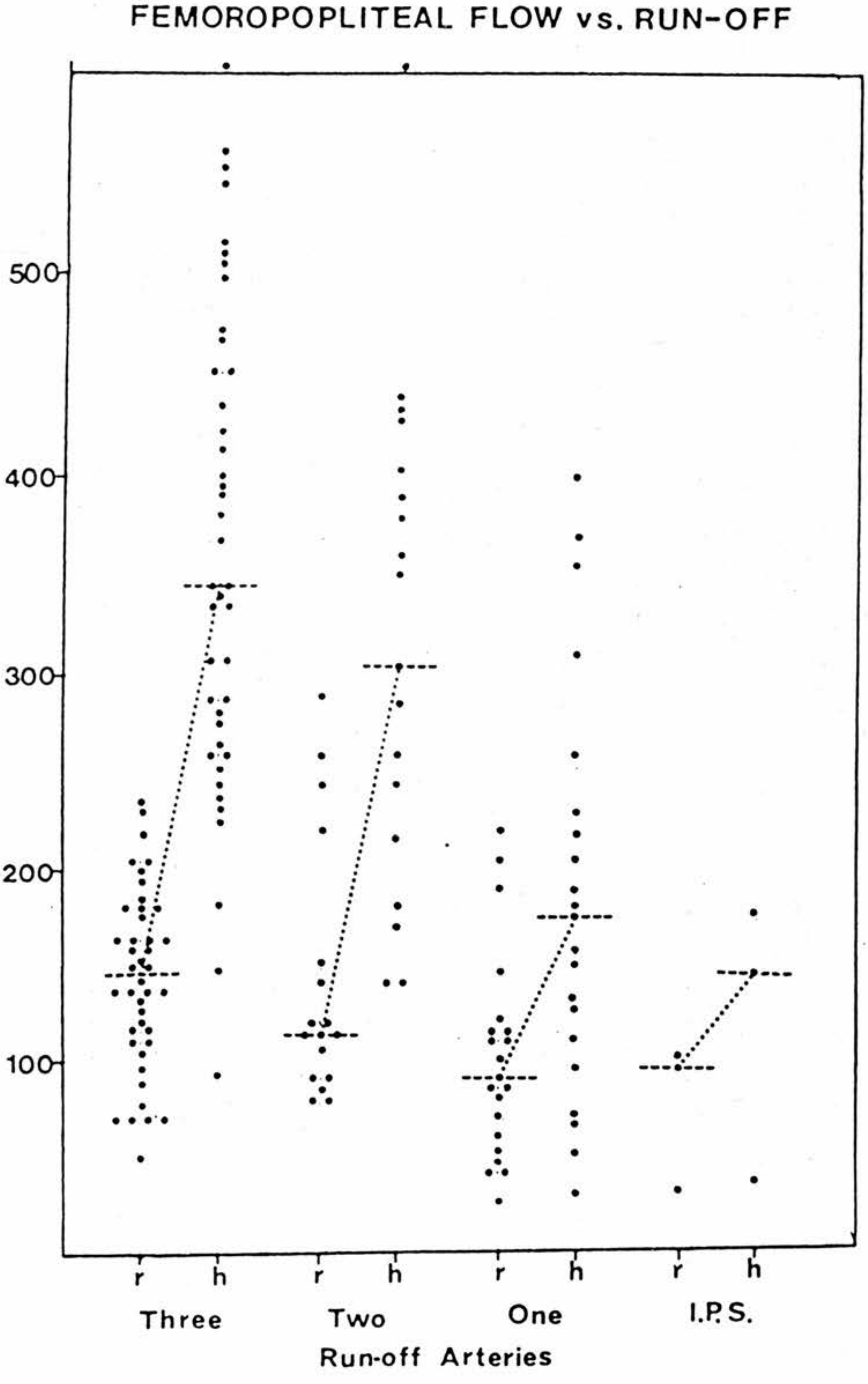


Figure 6.4: Mean values for resting (r) and hyperæmic (h) blood flow (ml/min), according to the number of patent calf arteries providing run-off as demonstrated by the pre-operative arteriographic assessment (I.P.S.= isolated popliteal segment). Median values indicated by broken lines.

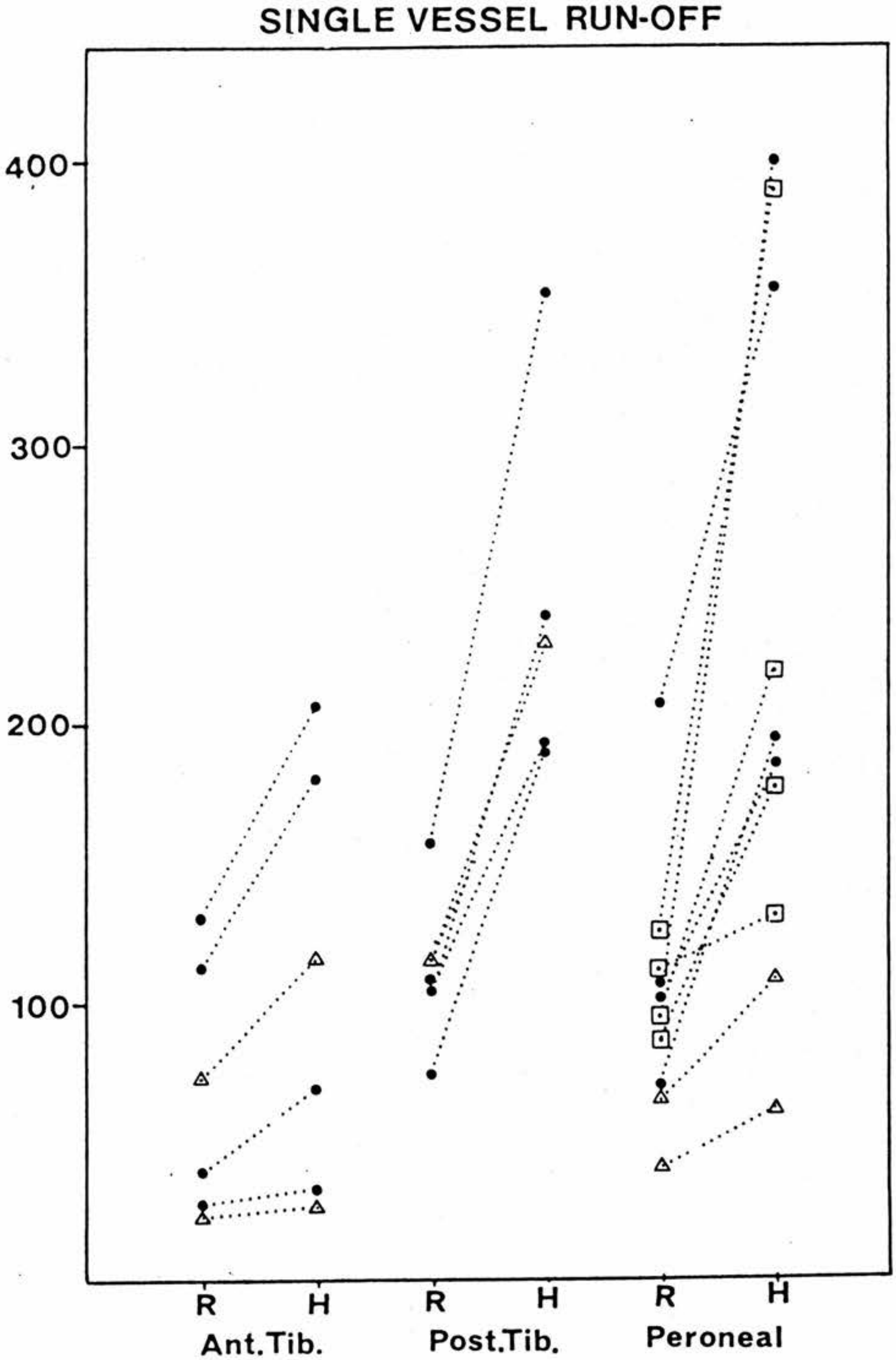


Figure 6.5: The resting (r) and hyperæmic (h) blood flow for bypasses in which only one calf vessel provided run-off set out according to which vessel was patent. The values for resting blood flow are given, in ml/min, by the left ordinate, and for hyperæmic flow by the right ordinate. An anastomosis to the popliteal artery is represented by • , to the tibio-peroneal trunk by ⊡ and to a tibial artery by ▲ .

Bypass failure and occlusion

Nineteen bypasses occluded, or required surgery to prevent occlusion, within 6 months of study. Of these, 3 were from the established group and 16 from the newly implanted. Details of graft type and time from implantation are set out in table 6.5. Eight occlusions occurred in bypasses examined only once; the other 11 had been studied at least twice.

Table 6.5

The number of bypasses of each type occluding or requiring salvage surgery during the study, with the time, in months (median + range), to this event from operation and from the date of the immediately preceding examination

	n=	months since operation	months since last examination
established	3		
reversed vein	1	23	5
in situ vein	1	18	3
fabric	1	10	3
newly implanted	16		
reversed vein	1	6	5
in situ vein	10	5 [1-12]	4 [2-6]
fabric	5	6 [2-11]	3 [2-6]

In 6 cases (4 fabric grafts and 2 saphenous vein) the preceding assessment had been entirely satisfactory both clinically and by all non-invasive criteria, and the occlusion was regarded as unexpected. Four of these cases had been studied twice. Thrombotic occlusion following transient stoppage of the bypass by kinking at the knee is considered a likely cause of these failures. Although not clearly demonstrated in any of these 6 unanticipated occlusions, kinking of both fabric and vein grafts at the level of the knee joint was seen using real-time imaging, and in the case of one femoropopliteal bypass caused a >50% reduction in blood flow.

In the remaining 13 occlusions, 7 of which had been studied at least twice, at least one indicator of abnormal or suboptimal function had been apparent in the preceding examination. These included symptoms of ischæmia, low resting or hyperæmic flow, low ankle systolic pressure index after exercise and low blood flow velocity. In the case of the 7 bypasses which were studied on at least 2 occasions prior to occlusion, a falling off of function was evidenced by a deterioration in one of these indices between the examination preceding occlusion and that 6 months earlier.

A poor reactive hyperæmic response (peak flow <120ml/min or <150% of resting flow) most accurately predicted subsequent bypass failure after a single measurement. A low peak systolic blood flow velocity (<30 cm/sec), low resting blood flow (<60 ml/min) and low post-exercise A.B.P.I.(<0.8) were also reliable indicators (table 6.6). Where failure occured of a bypass examined at least twice, a ≥33% fall in post-exercise A.B.P.I. proved the most accurate predictive index of occlusion (table 6.7). Changes in resting blood flow and resting A.B.P.I. proved considerably less accurate predictors than stressed measurements, emphasising the great importance of performing hæmodynamic tests in the lower limb under conditions of physiological stress.

Table 6.6

	sensitivity	specificity	mean accuracy
peak flow <150% of resting	58%	97%	87%
hyperæmic flow <120 ml/min	37%	97%	84%
peak flow velocity <30 cms/sec	37%	97%	84%
resting blood flow <60 ml/min	42%	95%	79%
hyperæmic flow <150 ml/min	63%	92%	81%
hyperæmic flow <200 ml/min	80%	88%	78%
A.B.P.I. <0.8	80%	85%	77%
peak flow <200% of resting	80%	85%	77%
peak flow velocity <40 cms/sec	58%	85%	72%

The sensitivity, specificity and accuracy of non-invasive measurements as predictors of occlusion of femoropopliteal bypasses following a single examination.

Table 6.7

	sensitivity	specificity	mean accuracy
fall in exercised A.B.P.I. ≥33%	36%	98%	84%
fall in hyperæmic flow ≥50%	57%	96%	78%
fall in exercised A.S.P.I. ≥25%	45%	94%	75%
fall in hyperæmic flow ≥33%	45%	90%	69%
fall in resting flow ≥50%	33%	92%	66%
loss of peripheral pulse	36%	90%	65%
fall in resting flow ≥25%	55%	69%	58%
new symptoms	64%	56%	56%
fall in resting A.S.P.I. ≥33%	55%	60%	55%

The accuracy in predicting occlusion of various indices demonstrating a deterioration in bypass function between 2 six-monthly examinations.

Mean blood flow velocity

The mean velocity at peak systole as measured from the resting flow waveform was 55 [10-115] cm/sec overall. For those 19 bypasses which subsequently occluded, the velocity was significantly lower (35 [10-90] cm/sec)($p<0.001$, $z=3.9$, Mann Whitney).

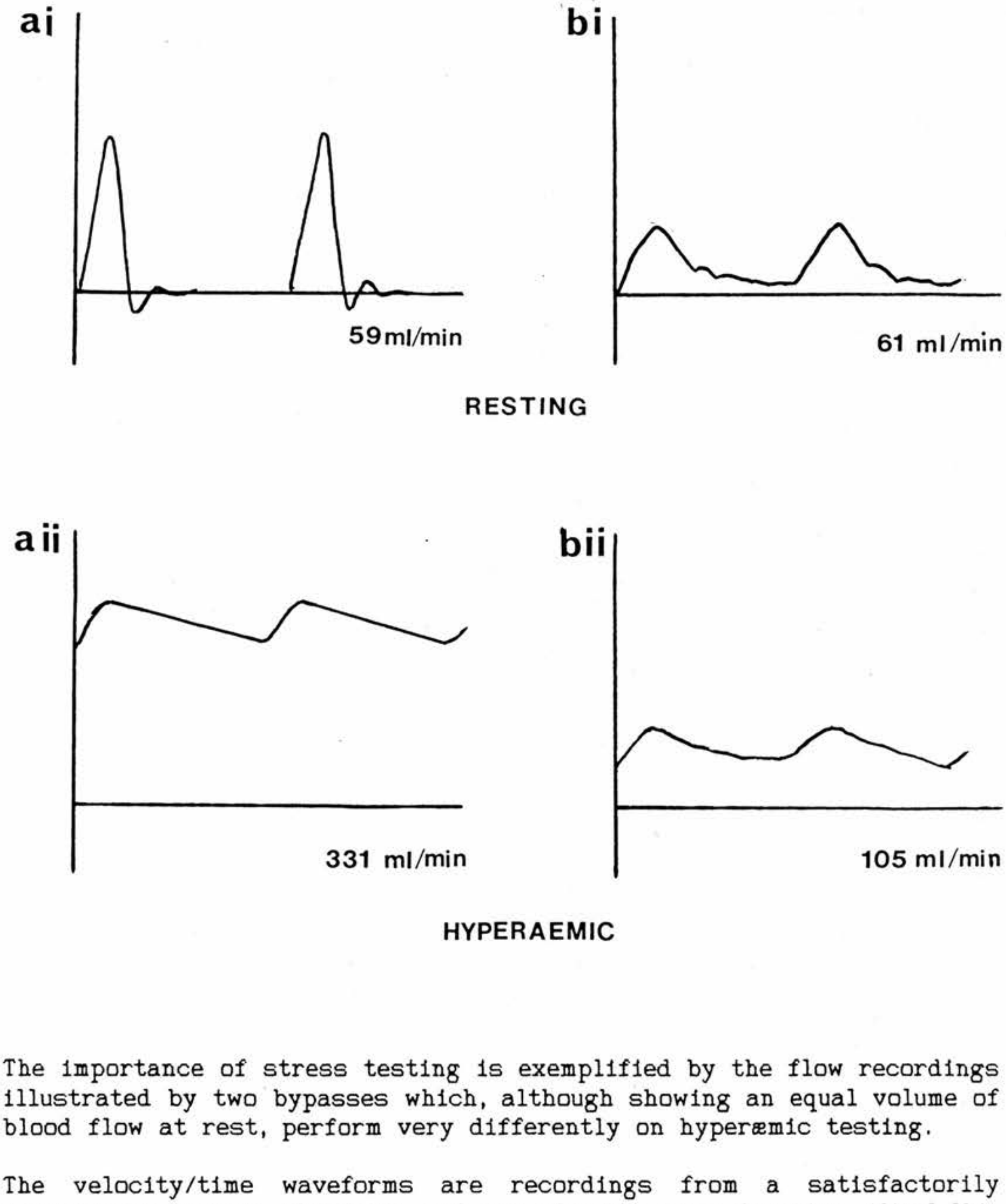
Low resting blood flow

Early in the study a resting blood flow of <80 ml/min, or even <100 ml/min was regarded as an index of relatively poor function. Later, it was noticed that a number of satisfactorily functioning bypasses showing a relatively low blood flow at rest, were capable of very satisfactory flow enhancement during reactive hyperæmia. Resting flow values of ≤100ml/min were recorded in 38 bypasses, ≤80ml/min in 21 and ≤60ml/min in 11, of which 8 subsequently failed. There was only one occlusion, however, in the group with resting flow values in the range 61-80ml/min. That a bypass conveying only 59 ml/min at rest is capable of satisfactory function is demonstrated in fig 6.6, where it is compared with another bypass which, although it showed similar resting flow, demonstrated markedly inferior function in other regards, and went on to occlusion.

Effect on blood flow of bypass graft luminal diameter

Resting blood flow showed a relatively low correlation with mean diameter for each bypass ($r_s=0.32$, $t=4.0$, $p<0.001$), but the correlation of peak hyperæmic flow was more striking ($r_s=0.54$, $t=7.6$, $p<<0.001$). But, although this would suggest that a narrow calibre bypass would be incapable of adequate function as a result of its reduced capacity for enhanced flow, it should be pointed out that, in 8 of the 24 bypasses with a luminal diameter ≤ 4mm, flow values in excess of 400 ml/min were recorded during hyperæmia.

figure 6.6



The importance of stress testing is exemplified by the flow recordings illustrated by two bypasses which, although showing an equal volume of blood flow at rest, perform very differently on hyperæmic testing.

The velocity/time waveforms are recordings from a satisfactorily functioning bypass (fig.6.6a) and one showing poor function (fig.6.6b). Although the resting blood flow is similar in both cases, in 6.6b this is reached only by continuous flow of blood throughout diastole. During hyperæmic testing, the bypass 6.6a conveys a very satisfactory enhanced blood flow more than 500% of the resting value, whereas in the bypass 6.6b flow rises to less than 200%. The poorly-functioning bypass went on to occlusion.

Discussion

Of all arterial reconstructions, femorodistal grafts have the poorest long term record. Once they thrombose it is seldom possible to re-establish flow in them, making important the careful monitoring of such reconstructions to detect failing function before occlusion occurs. What are the indicators? Although recurrence of symptoms, loss of pulses or falling ankle pressures have long been used, the detection rate of problem bypasses is low. Despite Szilagyi's study (1973), regular angiography is not feasible for regular follow-up. Although digital subtraction angiography (D.S.A.) offers a more realistic alternative, the quality of the images is not always of a satisfactory quality. Hitherto, flow measurements have been limited to peroperative electromagnetic studies, which have proved predictive of success only in the early postoperative period. Modern ultrasonic technology has made possible the study of blood flow in established bypasses, and provides a routine means of following up femoropopliteal reconstructions.

Duplex scanning of femoropopliteal bypasses is made easy by their relatively superficial location, facilitating reproducible and reliable flow measurements. The importance of measuring blood flow in femoro-popliteal reconstruction was appreciated early, and electromagnetic flowmeters have been used to measure blood flow in such bypasses per-operatively for over 25 years (Cannon *et al*, 1960; Cappelan and Hall, 1967; Little *et al*, 1968). Critical values have been described, below which there was a high probability of early failure of the bypass. Many authors (including Cappelan and Hall, 1967; Terry *et al*, 1972; Dedichen, 1976a; Sonnenfeld and Cronestrand, 1980) found a higher occlusion rate in the early postoperative period in those bypasses with a flow rate of <100 ml/min as measured immediately after completion of the reconstruction. Dean *et al* (1975) found that all bypasses with a flow rate ≤70 ml/min occluded, whereas, for Little *et al* (1968), 60 ml/min seemed to be a critical level, with an 80% early occlusion rate for bypasses with flow rates less than this, and 80% patency with higher flow rates. A low blood flow at rest does necessarily suggest poor function; in the present study, several grafts which conveyed considerably less than 100ml/min at rest were associated with normal ankle pressures, confirming the findings of Mannick and Jackson (1966). The widely ranging values for basal flow rates (for example, 17-130ml/min reported by Barner *et al* (1974); 80-200ml/min by Cappelan and Hall (1967)) perhaps suggest that to identify an absolute level of resting blood flow critical for long term patency measured intraoperatively by this, or any other technique is too simplistic. Indeed, several authors (including Mannick and Jackson, 1966; Barner *et al*, 1974; Shionoya *et al*, 1983) could identify no correlation between intraoperative flow values and early occlusion rates. Some authors have used papaverine to induce hyperæmic flow intraoperatively, and poor flow values in response to papaverine were claimed by Sonnenfeld and Cronestrand (1980) to be predictive of late occlusion, that is, beyond 3 months from insertion.

Blood flow and ankle systolic pressure indices.

The disadvantage of flow measurements has been that they have, with certain exceptions (for example, Renwick *et al.*, 1968; Cronestrand and Elekström, 1970; Hall, 1969), largely been limited, by the nature of the electromagnetic flowmeter, to peroperative studies alone. Ankle systolic pressures, generally expressed as a ratio of the brachial systolic pressure (A.B.P.I.), are used widely in the follow-up assessment of patients with arterial reconstructions. Corson *et al* (1978) found that an immediate postoperative A.B.P.I. of less than 0.7, or an increase of under 0.4 compared with the preoperative A.B.P.I. were both predictive of early failure. Laing *et al* (1983) used an A.S.P.I. measured after a one-minute exercise test to detect suboptimal function in 16 of 30 asymptomatic post-reconstruction patients, and proposed such testing as a means of identifying the bypass in danger of failure before symptoms develop. Certainly in the present study, and despite contrary evidence (Sampson *et al*, 1985; Shionoya *et al*, 1983), the stressed A.B.P.I. proved almost as efficient as poor flow measurements in the detection of a failing bypass, and a substantial deterioration in the post-exercise A.B.P.I. proved the single most reliable method of predicting occlusion in those bypasses examined on at least 2 occasions. This was substantially the finding of Taylor and Fox (1977), who proposed serial ankle pressure measurements as a sensitive means of detecting high risk bypasses. The close correlation of post-exercise A.B.P.I. and hyperæmic blood flow as demonstrated in the present study, suggests that, although imparting less precise information regarding blood flow, A.B.P.I. provides a simple and reliable means of assessing the adequacy of function of femoro-popliteal bypass.

Hyperæmic blood flow

The present study demonstrated that flow during reactive hyperæmia proved to be the best index for identifying the bypass in danger of occlusion. Although a substantial fall in the postexercise ankle pressure index between six-monthly examinations proved the single most accurate method of detecting a failing bypass, the resting ankle pressures were of much less value. The response to hyperæmic testing can, to some extent, be predicted from the resting Doppler flow waveform, as shown in figure 6.6. In both examples the resting flow is around 60ml/min. The top example is from a satisfactorily functioning bypass, the lower from a poorly functioning bypass which occluded within three months of the examination. In the top example, the Doppler shift waveform shows a steep rise and fall of blood flow velocity in systole, followed by a short reverse flow wave and minimal flow in diastole. It resembles, quite closely, the triphasic waveform of a healthy femoral artery. The lower example, however, shows a much less steep rise and fall of the systolic flow wave followed by a persistent low velocity flow throughout diastole, of a form associated with peripheral vasodilatation. A waveform of this type was quite commonly seen at rest in the immediate postoperative period, or during hyperæmic testing. Following release of the occluding cuff, the blood flow increases, as described in Chapter Four, with a relatively small increase in systolic velocity, but a large increase in diastolic velocity, so that most of the extra blood flow occurs during diastole. This is clearly demonstrated in the peak hyperæmic flow waveform in the successfully functioning bypass (fig 6.6 [aii]), with a greater than 500% increase in the resting flow. Since flow was present throughout diastole in the failing bypass in order to meet flow requirements at rest (fig 6.6 [bi]), any extra peripheral vasodilatation after release of the occluding cuff was very small, and the resulting hyperæmia suboptimal (fig. 6.6 [bii]).

Blood flow velocity

Bandyk *et al* (1985) related early postoperative graft occlusion to a peak systolic blood flow velocity of <40 cm/sec. A significantly lower peak velocity was certainly demonstrated in the present study in those bypasses which subsequently failed, but a level of 30cm/sec proved more accurate than 40 cm/sec as a critical value for the prediction of bypass failure. A high peak flow velocity at rest was generally associated with a waveform of the shape of that in figure 6.6 [ai], with a rapid acceleration and deceleration of the systolic wave, whereas a slowly rising and falling systolic wave, as in figure 6.6 [bi], was almost invariably associated with a very poor peak flow velocity. Kouchoukous (1967) had noticed the predictive importance of flow waveforms of these types. He correlated a rapid upstroke and downstroke with success, whereas bypasses showing the slow rise and fall pattern of systolic flow were associated with a greater than 50% early occlusion rate. The peak velocity is of more interest in this regard than the mean velocity; in figure 6.6 the mean velocity averaged throughout the cardiac cycle was greater in the poorly functioning bypass (fig 6.6 [bi]). It has been suggested that a rapid velocity is more crucial for the continued patency of fabric rather than autogenous vein grafts: Sauvage *et al* (1971) have put forward the idea that a critical level of blood flow velocity is required to prevent the deposition of thrombus in a synthetic bypass.

Unexpected failure

In 6 cases, occlusion unexpectedly occured in a bypass previously showing no features of suboptimal function. Four of these 6 were fabric grafts (3 polytetrafluoroethylene and 1 woven Dacron). A likely cause of a sudden thrombotic occlusion might be the obliteration of the bypass lumen by kinking at the knee (Baddeley *et al*, 1970, Clifford *et al*, 1981). In all 6 cases the lower anastomosis was to the infragenicular part of the popliteal artery, and this is a probable cause for the occlusions.

Postoperative hyperæmia

In the 19 patients who were studied within 2 weeks of surgery, the blood flow at rest was significantly greater than in the same bypasses when studied 6 months later. There was no such difference in the peak hyperæmic flow. In 17 of these the resting blood flow waveform showed forward flow throughout diastole, which disappeared on subsequent examination. In other cases in whom persistent diastolic flow was observed this was taken to be an abnormal feature. In 3 cases it resulted from a patent arteriovenous fistula in *in situ* bypasses in which venous tributaries had been left unligated. In these cases continuous blood flow throughout the cardiac cycle was observed in the bypass proximal to the fistula; below the fistula, a more usual pattern was observed with flow during systole only, but a much smaller total volume of blood flow. In other cases, a bypass which required diastolic forward flow to maintain the circulatory needs of the distal extremity at rest was always associated with poor function on hyperæmic testing (fig 6.6 [b]).

Correlation of blood flow with state of arterial run off.

In the present study a marked correlation was found between blood flow, both at rest and hyperæmic, and radiological demonstration of arterial run off, confirming the results of others (Mannick and Jackson, 1966; Barner, 1968; Cronestrand, 1970). Although some authors (for example Bernhard, 1971) claim that the site of the distal anastomosis does not influence flow rates, the findings of the present study correlate with those of Bandyk *et al* (1985). Poor flow values are generally associated with run-off to an isolated popliteal segment or to a tibial vessel. Moreover, where only one artery provides run-off, the flow rates are significantly better in those cases in which a popliteal anastomosis was carried out than where the anastomosis was directly to the patent tibial artery.

Contrary to the experience of Armour *et al*, 1976, the anterior tibial artery seemed to contribute least to run off in the present series. In those grafts where this vessel provided the sole run off flow was significantly less than that measured in comparable patients in whom the peroneal or posterior tibial artery alone were patent; in the 12 patients in whom an anterior tibial occlusion permitted the lower anastomosis to the tibio-peroneal trunk, the flow was not significantly different from those in which all 3 vessels provided run off.

Summary

Ultrasonic flowmetry proved reliable and easy in femoropopliteal bypasses, and was eminently suitable for use in routine follow-up of patients with these reconstructions.

Flow measurements showed correlation with symptoms, and with ankle pressure systolic pressure indices; the correlation was more marked when enhanced flow values were considered.

The blood flow was significantly greater where at least two calf arteries provided run-off.

A greater than 100% increase in resting blood during a standard reactive hyperæmia test proved a reliable index of satisfactory function, even when resting flow levels were low.

Enhanced blood flow during reactive hyperæmia proved the single most reliable method of predicting bypass failure, although, with careful regular follow-up, a deterioration in post-exercise ankle pressure index was as reliable in predicting occlusion.

Chapter Seven

Luminal diameter changes in implanted Dacron bypasses

Introduction

Changes in the calibre of a bypass after implantation are potentially important, since graft stenosis, dilatation and aneurysm formation can result in impaired function.

In order to assess changes in the diameter of fabric arterial prostheses after implantation, 219 fabric bypasses in 131 patients were studied using the high resolution B-mode imaging system of the Technicare scanner. Generalised and localised dilatations were looked for, and anastomoses carefully examined for false aneuryms. Measured diameters, expressed as a ratio of the manufacturers' stated diameters, were compared for 3 types of Dacron prosthesis.

Patients and methods

The total number of grafts and graft limbs, with time from implantation to study, were as follows:-

Table 7.1

	Vascutek$^{\rho}$	Meadox$^{\sigma}$	U.S.C.I.$^{\tau}$
Aortobifemoral (177 limbs)	68	80	29
iliofemoral (n=10)	3	5	2
femorofemoral (n=31)	6	8	17
femoropopliteal (n=1)		1	
total	77	94	48
time from implantation (months)	8 [1-20]	26 [3-62]	13 [1-38]

ρ : Vascutek knitted Dacron, high porosity, 1200 mls/cm^2/sec
σ : Meadox double velour knitted Dacron, high porosity, 1400 mls/cm^2/sec
τ : U.S.C.I. Debakey woven Dacron

All patients were examined in a supine position with the ultrasonic transducer hand-held. Aortofemoral and iliofemoral bypasses had diameter measurements performed on the iliac portion of the bypass by placing the transducer in the inguinal crease and directing it cephalad. Femorofemoral bypasses were best imaged in the suprapubic region, although a trans-sonic gel "stand off" was occasionally required to bring the bypass within the focal range of the transducer, especially in lean patients. It was possible, however, to visualise the entire length of femorofemoral and femoropopliteal bypasses, and the femoral anastomoses of all bypasses was studied for possible anastomotic false aneurysms.

At least 5 measurements of bypass diameter were made using the electronic calipers from a magnified frozen image of a longitudinal section of each graft. Under image magnification, reproducibility to within 0.5 mm was possible. The presence of a circular lumen was checked by rotating the transducer until a transverse sectional view was obtained. The measured diameters were then compared with the manufacturers' stated internal diameters. Areas of local dilatation were noted.

Results

In all but 7 cases, the knitted bypasses preserved a regular luminal diameter, with minimum tissue deposition. In 3 cases, local prosthetic dilatation was observed (fig 7.1). In 3 other cases, anastomotic dilatation or false aneurysm formation was present, in one case involving both anastomoses of a femorofemoral bypass. In the remaining patient one limb of a bifurcated graft was considerably narrowed by kinking as it passed under the inguinal ligament. (fig 7.2).

In woven grafts the luminal coating of the vessel wall was noticeably thicker than in the knitted group. In some cases this produced a narrowed lumen. No dilatation or true aneurysm formation was present.

In table 7.2 and figure 7.3 are set out diameter ratios (that is ultrasonically measured diameter of implanted bypass divided by the manufacturers' stated diameter) for each of the 3 groups of Dacron grafts. The slight increase in diameter seen in the Meadox bypasses was significantly greater than that observed in the Vascutek ($p<<0.001$, $z=5.3$, Mann Whitney). The luminal narrowing observed in woven grafts produced a diameter which was highly significantly less than that seen in the knitted groups ($p=<<0.001$, $z=7.3$, Mann Whitney). Although the significantly longer interval between implantation and study for the Meadox grafts compared with Vascutek (table 7.1) might explain the greater degree of dilatation seen in the former, the correlation of diameter ratio with time from implantation for Meadox grafts was not high ($r_s = 0.13$).

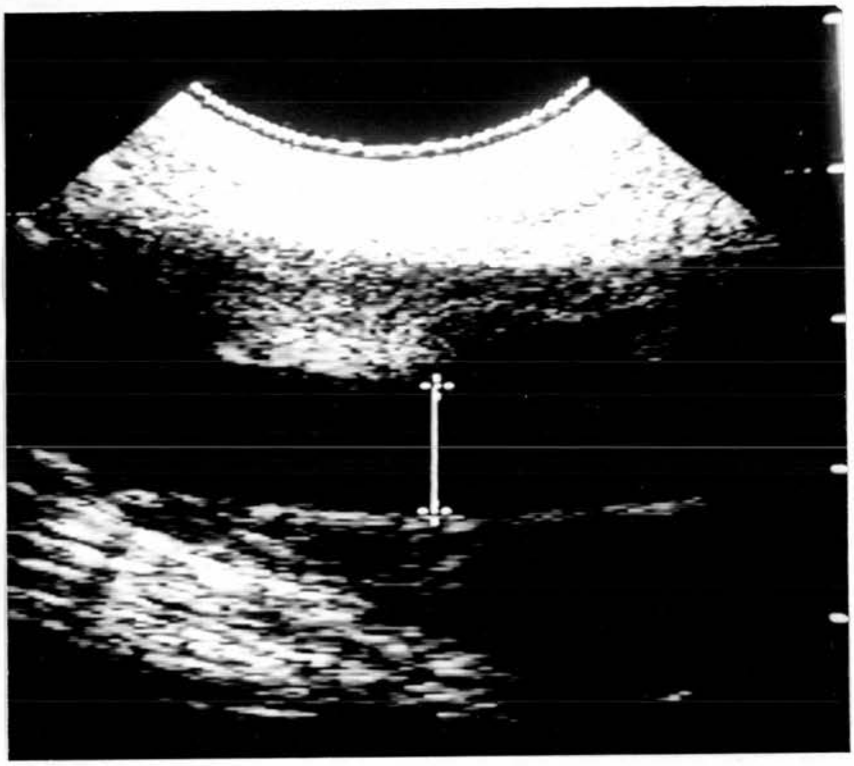
Localised areas of fabric dilatation to >150% of the diameter at implantation were observed in 3 bypasses. In all 3 cases the material involved was double velour knitted Dacron. In one case, a femoropopliteal bypass (fig 7.1), the maximum diameter of the aneurysm was more than 3 times the original diameter at implantation. The other cases were an iliofemoral bypass and an aortofemoral bypass limb. In all 3 cases, the mean diameter of the non-aneurysmal portion of the graft was more than 115% of the diameter at implantation. In all cases the reconstruction had been undertaken more than 4 years earlier.

Anastomotic false aneurysms were seen at 4 anastomoses between the femoral artery and prosthesis. In 2 cases the femoral limb of a bifurcated aortobifemoral graft was involved. The other case involved both anastomoses of a femorofemoral crossover bypass graft. Two of these bypasses were of knitted Dacron, and the other of woven Dacron. The prevalence of anastomotic false aneurysm in the present study was 1.6 per 100 anastomoses studied.

Table 7.2

Values (median and range) of $\frac{\text{measured diameter}}{\text{original diameter}}$ x 100% for the 3 types of bypass

Knitted prostheses	
Meadox (Cooley double velour)	107% [74-144%]
Vascutek 1200	100% [82-114%]
Woven prostheses	
U.S.C.I. DeBakey	80% [37-104%]



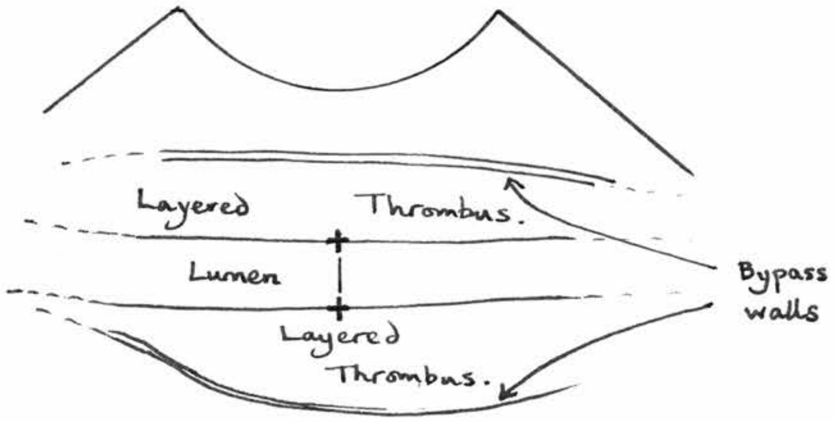
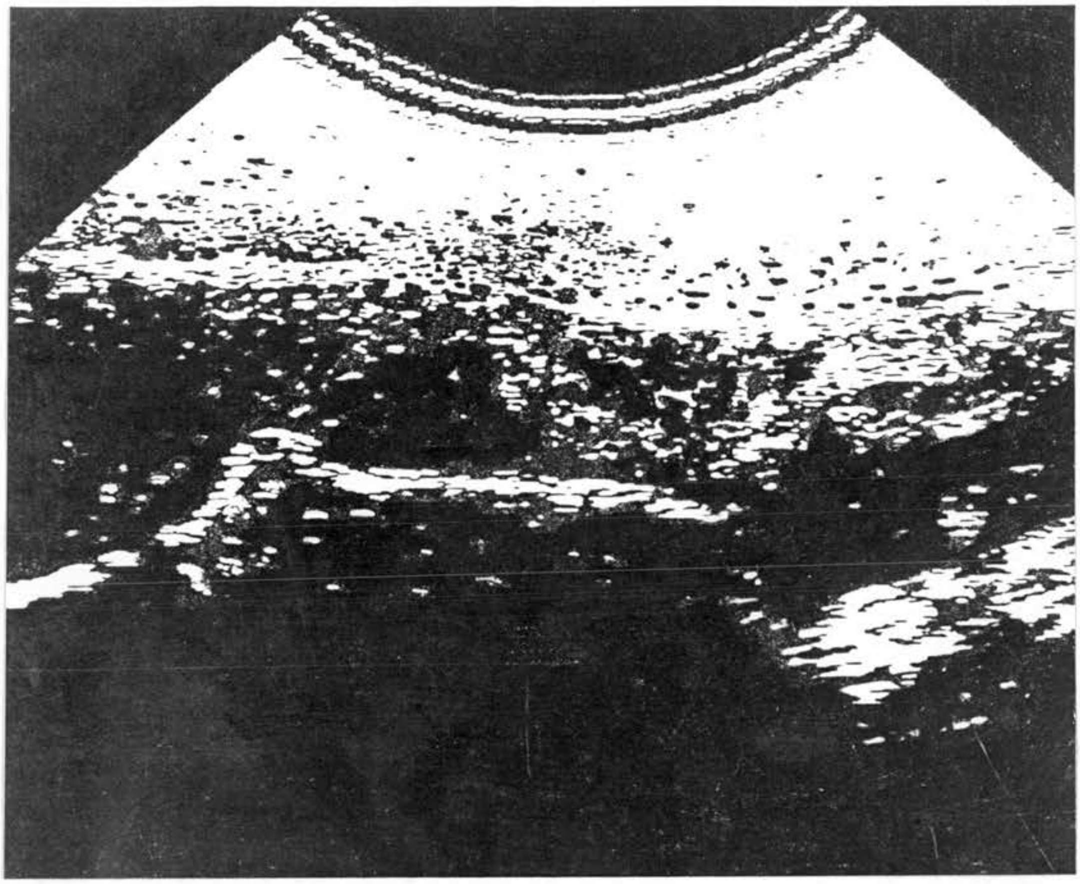


Figure 7.1: Aneurysmal dilatation of a double velour Dacron femoropopliteal prosthesis 6 years after insertion.



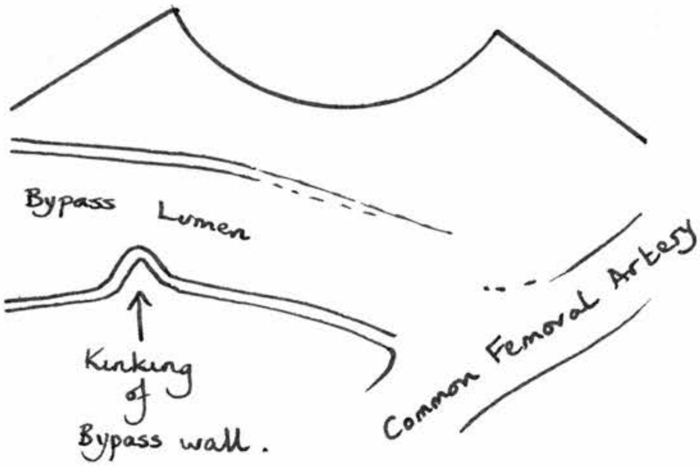


Figure 7.2: Reduction of the lumen of one limb of an aortofemoral bypass due to kinking of the posterior wall as it passed under the inguinal ligament. This limb subsequently occluded.

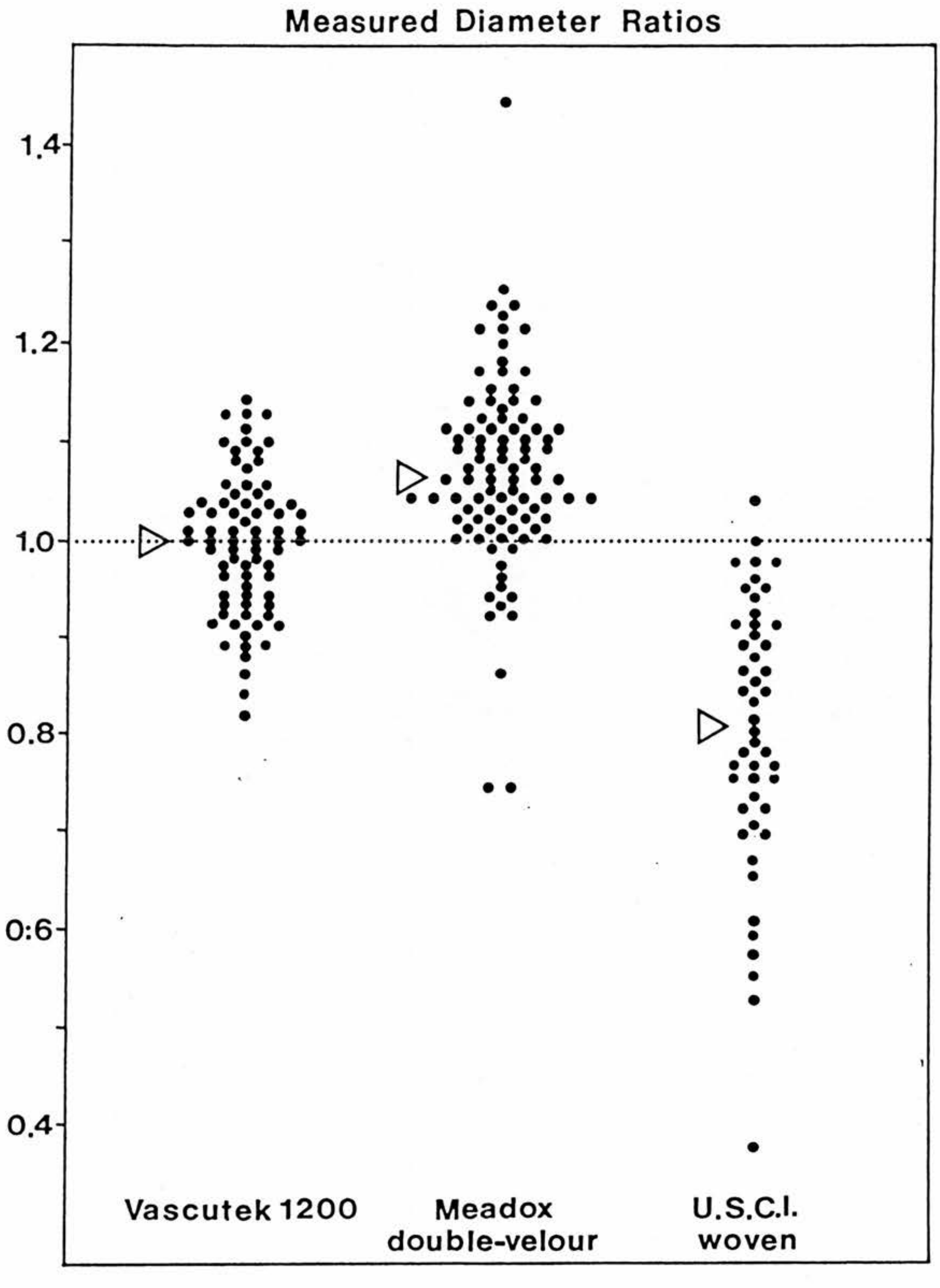


Figure 7.3: Mean diameter measurements, expressed as a ratio of the manufacturers' stated diameter, for the 3 types of Dacron prosthesis studied. The median values are arrowed.

Discussion

A good match in the calibre of a graft and the artery to which it is anastomosed has already been mentioned as an important requirement for efficient functioning of a bypass. It is essential that the graft should preserve, as far as possible, its original dimensions after exposure to arterial pressure and tissue incorporation. Clearly, a graft which suffers progressive narrowing of the lumen by tissue encroachment is liable to thrombosis, but a bypass which has dilated excessively is also in danger of occlusion. A substantial increase in diameter brings about a sharp fall in blood flow linear velocity and an increase in turbulence with a consequent risk of thrombosis (Greenhalgh, 1981).

Graft dilatation is generally one of the following:

(a) A generalised and proportionate increase in overall diameter
(b) A localised dilatation or aneurysm formation
(c) Anastomotic false aneurysm formation

Generalised dilatation

A generalised increase in prosthetic bypass calibre has been reported by clinicians and investigated *in vitro* by manufacturers. In their invesigation of the dynamic compliance of Dacron grafts implanted in dogs, Baird *et al* (1977) noted an increase in diastolic diameter of 5%, 2 weeks after implantation. Kim *et al* (1979) reported a progressive increase in luminal diameter over a period of about 30 days after implantation, after which little further dilatation, if any, occured. The 15% mean increase in diameter of Dacron aortic bypasses, measured by Nunn *et al* (1979) using an ultrasonic technique, increased to 21% in those patients who were hypertensive. These figures are very similar to the expected dilatation derived *in vitro* by U.S.C.I. (<25%) and Meadox (10-22%) (Nunn *et al*, 1979). Nunn expressed the view that Dacron grafts as a whole tend to dilate early after implantation and the dilatation slowly increase with time thereafter. He described 3 components to this generalised dilatation:

1) an increase in graft diameter and length due to a flattening out of the crimping as the graft is inflated by blood under arterial pressure

2) an increase in diameter at the expense of length due to a rearrangement of the textile structure

3) an increase in diameter due to a deformation of the basic graft material.

The 7% increase in luminal diameter observed in double velour knitted grafts in the present study is very much in keeping with the degree of dilatation described by these and other authors. The poor correlation of incremental diameter increase (100% x measured diameter/original diameter) with time from implantation supports the view that most of the dilatation occurs shortly after the implanted prosthesis is exposed to arterial blood pressure. Clagett *et al* (1983) also found a poor correlation between incremental dilatation and time from implantation. Their suggestion that this early, and inevitable, dilatation is a function of reorganisation of the knitted fabric rather than a stretching of the yarn itself seems most plausible. On the other hand, all 3 bypasses in which aneurysmal dilatation was observed in the present study, had been implanted for more than 4 years.

Aneurysmal dilatation

There have been several reports of aneurysmal dilatation of Dacron prostheses leading to bypass failure, but these represent only a minute proportion of the large number of such grafts actually inserted. Early in the history of prosthetic development, Helenca compliant grafts so frequently underwent gross dilatation that they had to be abandoned. Although many reports of aneurysmal dilatation and rupture involved light-weight knitted prostheses no longer in general usage (Ottinger *et al*, 1976; Blumenberg and Gelfand, 1977), isolated examples of excessive dilatation have been reported in standard weight knitted (Cooke *et al*, 1974), woven (Knox, 1961) and double velour knitted (Nucho and Gryboski, 1984) Dacron prostheses. The problem is not confined to Dacron grafts. Aneurysmal dilatation has been reported in polytetrafluoroethylene (Campbell *et al*, 1976;

Roberts and Johnston, 1978) and human umbilical vein (Dardik *et al*, 1984) prostheses.

Focal areas of dilatation presumably have a different aetiology from the uniform generalised dilatation discussed earlier. Berger and Sauvage (1980) and Yashar *et al* (1978) have incriminated focal defects, such as broken yarn or deterioration and fragmentation of Dacron fibres, resulting from damage to the prosthetic material prior to implantation rather than to an intrinsic deterioration of fibres following implantation. Clagett *et al* (1983), however, found no evidence of fracture, distortion or thinning of individual filaments on scanning electron microscopy, nor any reduction in breaking strength of Dacron from excised portions of dilated bypasses compared with normal. Their most striking findings were of generalised looseness and loss of compactness of the involved fabric, suggesting that yarn slippage due to a defect of manufacture is the likely cause of regional dilatation.

Although no increase in overall diameter was found in hypertensive patients, all 3 of the Dacron bypasses which showed aneurysmal dilatation in the present study were inserted in patients in whom diastolic blood pressures greater than 100 mmHg had been recorded preoperatively. Despite the degree of dilatation, all 3 bypasses showed satisfactory function, and in no case was it found necessary to excise a bypass. In the case of the aneurysm occuring in a femoropopliteal graft (fig 7.1), the luminal diameter was little different from that in the non-dilated portions of the graft, the bulk of the graft lumen being filled with layered thrombus. Under these circumstances, of course, arteriography would fail to deliniate the degree of dilatation of the affected segment.

Luminal narrowing in woven prostheses

The tightness of the weave in a woven Dacron bypass minimises yarn slippage when the fabric of the graft is expanded, probably accounting for the comparative rarity of reports of dilatation of woven prostheses (Knox, 1961). Certainly no overall dilatation was observed in any woven graft in the present study. Tissue encroachment upon the lumen of these bypasses was considerably more than in the knitted grafts; in very few of the latter was the tissue layer visible using the B-mode ultrasound, implying that it was <0.5 mm in thickness. The grey scale of the B-mode ultrasound was of sufficiently high resolution to separate images of graft wall fabric and tissue deposit. In earlier duplex scanners this facility was less developed, although some authors have used, in combination, B-mode and ultrasonic flow imaging to estimate luminal narrowing (Baird *et al*, 1979). The tightness of the weave prevents excessive intraoperative blood loss However, ingrowth through the wall of the bypass resulting in the inner fibrin layers is less well organised and the capsular bonding less firm than in with more porous materials. Although making re-exploration easier than for more tightly incorporated material, perhaps this property is responsible for the excessive luminal tissue deposition seen in some of these grafts.

False aneurysms

The most frequently reported complication associated with Dacron aortofemoral bypass grafts has been the development of anastomotic false aneurysms (Gaylis, 1981; Kim *et al*, 1979; Ottinger *et al*, 1976). It is generally agreed that the fabric of the prosthesis is not the culprit, but that the complication arises as a result of problems with the suture material or the host artery. False aneurysms have been easily detected by real time ultrasound (Gooding *et al*, 1981; Szilagyi *et al*, 1975). I have found precise measurement of the bypass diameter most difficult in the region of the femoral anastomosis, however. Since the lumen at this point consists partly of graft and partly of parent artery, it would seem unreasonable to diagnose an anastomotic aneurysm unless the diameter at the point of anastomosis be substantially greater than the sum of the diameters of the graft and of the donor artery. In 4 limbs anastomotic aneurysms satisfying this criterion were identified. In all 4 cases a palpable groin mass was present. But the technique proved useful in 2 further patients in whom groin masses suspected as anastomotic false aneurysms were found to be superficially placed, tortuous but non-dilated Dacron graft limbs. The graft diameters proximal to the anastomosis showed significant dilatation in 2 of the 3 cases. That anastomotic false aneurysms tend to be associated with bypasses which have dilated excessively was also the finding of other authors (Ottinger *et al*, 1976; Kim *et al*, 1979; Clagett *et al*, 1983). The prevalence of 1.6% found in the present study is within the range reported by other authors of 1-3% (Szilagyi, 1975; Gooding *et al*, 1981).

Surgical repair was undertaken in 3 of the 4 aneurysms. In each case the suture line was intact on the graft side of the anastomosis, and had cut out from the arterial side. This observation is made also by Clagett *et al* (1983) who propose that an abnormal dilatation of the bypass limb brings about abnormal tension and forces at the anastomosis which cause the sutures to tear out of the vessel wall.

Summary

Ultrasonic imaging permitted identification and measurement of graft stenosis and dilatation, including false aneurysms.

Knitted Dacron prostheses showed a tendency towards generalised luminal dilatation, although this was usually less than 10% and more pronounced in Meadox double velour than in Vascutek 1200 grafts. The lumina of woven grafts was generally narrowed by tissue encroachment.

Chapter Eight

Flow in aortofemoral and iliofemoral bypasses

Introduction

Aortofemoral and iliofemoral bypasses are generally effective and long-lasting. In only a small proportion of patients with severe multisegment disease do they fail to provide a good hæmodynamic improvement. Sometimes a combined proximal and distal reconstruction is required, either staged or at one sitting. The indications for adding a femoropopliteal bypass to a proximal reconstruction are controversial, being resorted to less frequently by some (Benson *et al*, 1966: Martinez *et al*, 1980; Crawford *et al*, 1981; Brewster *et al*, 1982 than by others (Dardik *et al*, 1979; Nevelsteen *et al*, 1980: Harris *et al*, 1985) The preoperative ankle pressure, the angiographic appearance of the profunda femoris artery run-off and the extent of gangrene of the foot are of limited value in predicting when a femoro-distal bypass will be necessary.

Based on the hypothesis that a poor clinical outcome might be associated with suboptimal graft blood flow, such a study was undertaken to see if worthwhile conclusions could be drawn.

Patients and methods

One hundred and seventy seven graft limbs were studied in 89 patients with aortobifemoral bypasses. The patients, of whom 21 (24%) were women, were aged 67 [41-82] years at the time of study. The period between implantation and study was 9 [1-62] months. Ten patients, 6 men and 4 women, aged 66 [50-89] years, with unilateral iliac artery disease, who had been treated by insertion of an iliofemoral bypass, were also studied. In 62 cases, the aortobifemoral bypass had been performed for aortoiliac occlusive disease, in 19 cases for rest pain and 43 for intermittent claudication. In the remaining 27 cases, an aortic aneurysm had been the indication for surgery. Of the 10 iliofemoral bypasses, 7 had been used for rest pain and the remainder for intermittent claudication.In the case of 31 limbs the graft was of knitted Dacron (U.S.C.I. DeBakey), and of knitted material in the remainder (71 Vascutek 1200; 85 Meadox double velour 1400)(see table 7.1, page 99)

Patients received a clinical assessment, and were examined using the duplex scanner and by ankle pressure measurements. After a 15 minute rest period, each limb of the bypass was imaged, and resting flow measurements made. This involved taking the mean of at least five measurements of the luminal diameter of the bypass made using magnification of a frozen real-time image (see Chapter Seven), and this was used to compute resting blood volume flow.

In 39 limbs of 27 patients with aortofemoral bypasses and in all 10 with an iliofemoral bypass, peak hyperæmic flow was measured following occlusion by a pneumatic cuff placed above the knee and inflated to 50mm Hg above systolic pressure for three minutes. Measurements of blood flow were made within 20 seconds of the rapid deflation of the cuff, and again at 30 seconds, in order that the peak hyperæmic flow value might be estimated. Although it had been intended to apply hyperæmic testing to all the limbs studied, in many cases patients were unable to tolerate a thigh cuff inflated to the appropriate pressure for as long as 3 minutes. Ankle systolic pressure indices were measured at rest and following the hyperæmic test.

Flow measurements were compared with patients' symptoms, arterial run-off and A.B.P.I..

Results

In the aortofemoral limbs, resting blood flow measurements were 258 [94-508] ml/min, rising by 319% [138-677%] to 827 [171-1790] ml/min in those examined with hyperæmic testing. In the 10 iliofemoral bypasses, resting blood flow rose from 238 [138-413] ml/min by 135% [73-290%] to 590 [173-1053] ml/min during peak hyperæmia. The ranges of flow for the two bypass types do not differ statistically.

In 105 limbs with a patent superficial femoral artery (S.F.A.), blood flow was significantly greater than those in which the profunda femoris artery alone provided run-off (figure 8.1). The differences applied both to resting blood flow (304 [125-508] ml/min versus 223 [94-414] ml/min; $p<0.0001$, Mann Whitney) and to hyperæmic flow

(970 [377-1790] ml/min versus 576 [171-1060] ml/min)(p=0.0.0002). A comparable difference was found in ankle systolic pressure indices (1.0 [0.47-1.2] versus 0.68 [0.35-1.1])(p<0.0001, Mann Whitney).

Resting blood flow and resting A.B.P.I. were compared in limbs with patent and occluded superficial femoral arteries. Where a S.F.A. provided run-off, the correlation between resting flow values and ankle pressure indices reached statistical significance (r_s=0.27, t=2.8, p<0.01). However this was not so where the profunda artery provided the only run-off (r_s=0.16, t=1.3, p>0.1).

Clinical outcome

Seventy-six patients were symptom-free with satisfactory resting flows of greater than 120 ml/min. Nine limbs had a resting flow of less than 120 ml/min and all gave rise to ischæmic symptoms. Rest pain was present in the one limb in which the resting flow was less than 50 ml/min. In 6 other patients, mild claudication was present despite apparently satisfactory resting blood flow. In all these cases, however, the superficial femoral artery was known to be occluded, and the measured hyperæmic blood flow, 182% [138-214%], and stressed ankle pressure indices, 0.56 [0.41-0.78], were markedly abnormal, suggesting that their symptoms were due to distal arterial disease, rather than to problems related to the bypass or proximal arteries.

Three bypasses occluded within one year of study. In one case, one limb of a bifurcated bypass occluded; its anastomosis was to a diseased profunda femoris artery, and low flow rates were present at rest and during hyperæmia (96 and 171 ml/min respectively). Moreover, B-mode examination demonstrated that the bypass was kinked as it passed under the inguinal ligament.(see Chapter Seven, figure 7.2). In the second case, both limbs occluded in a small calibre bypass (12/6½mm). Very poor resting and hyperæmic blood flow values were present. Subsequent reconstruction was carried out, using a new bypass graft, but function remained poor, the distal run-off being provided on both sides by a diseased profunda femoris artery. The third occlusion occurred in an elderly patient with an iliofemoral bypass which had shown poor function both at rest and during hyperæmia. One patient with a bifurcated graft required surgery for a false aneurysm of a femoral anastomosis.

The association of low flow rates with poor clinical results in patients with small vessels, severe ischæmia and multisegment disease raises the possibility of an improved outcome if reconstruction were extended to a more open outflow tract by the addition of a femoro-popliteal bypass.

Discussion

In the majority of cases, satisfactory flow rates were recorded, which closely match the normal values for resting and enhanced flow in the undiseased common femoral artery. As in the case of femoropopliteal bypasses, a good hyperæmic response was very reassuring where resting flow vaues were borderline, or where questionable symptoms of arterial insufficiency were present. Cotton *et al* (1972) demonstrated an increase in resting flow from 132±146 ml/min before reconstruction to 279±122 ml/min, measured by electromagnetic flow probe immediately after reconstruction. Hyperæmic flow, induced by papaverine, increased from 344±672 ml/min to 524±176 ml/min. These authors point out that a doubling of flow with papaverine provided evidence that there was no significant occlusive arterial disease upstream or downstream from the reconstruction. This emphasises one of the problems related to flow measurement in the aortofemoral graft limb, that is the effect that distal arterial disease has on graft outflow, and the difficulty in differentiating poor bypass function from problems relating to poor run-off. In general the results of the present study would suggest that, poor function of the bypass or of proximal inflow results in poor flow values both at rest and during hyperæmic testing. Distal disease, however, is associated with a relatively normal blood flow at rest, but poor response to hyperæmic testing. Resting ankle pressure indices did not distinguish well between these causes of poor clinical outcome.

Robbs and Wylie (1981) found that of 58 patients with aortofemoral bypasses reoperated upon, progressive atherosclerosis was the reason in 32 cases, involving the inflow arteries in 7 patients and the distal vessels in 25. In 7 patients, failure had been due to problems related to the graft itself; kinking in 3 cases, and problems related to mural thrombosis in the remainder. Of the 2graft failures during the course of the present study, a clear problem had been identified in one, in the form of the bypass kinking noted in Chapter Seven, but successful reconstruction, both in this case and in the only other case for which operation was required after limb occlusion, was prevented by progressive occlusive disease affecting the run-off vessels. Indeed, progressive disease of the outflow tracts was found to be the greatest cause of suboptimal function of aortofemoral bypass by several authors (including Brewster and Darling, 1978;, Malone *et al,* 1975; Mulcare *et al*, 1978).

The only difficulty proved to be the measurement of hyperæmic blood flow; many patients found the above-knee position for the pneumatic cuff too painful to endure for the prescribed 3 minutes. A below-knee cuff or a shorter period of occlusion might have been better tolerated but, as discussed in Chapter Four the resulting hyperæmia, being reduced and of shorter duration, is perhaps less suitable for comparative purposes. Taken in conjunction with the information available from real-time imaging, however, ultrasonic flow measurement provides a reliable method of identifying poorly functioning aortofemoral reconstructions, and selecting those which might benefit from further investigation by arteriography or digital subtraction angiography.

As in the studies reported in earlier chapters, flow in aortofemoral bypasses correlated with clinical symptoms and demonstrated the beneficial effect of improved arterial run-off. Flow was relatively easily measured in aortofemoral bypass limbs, although the technique proved more difficult to learn than that required for femoropopliteal bypass. In the case of all 3 failures, abnormally low blood flow had been recorded and in one case, a potentially remediable cause in the form of a narrowing of the bypass lumen due to kinking had been identified using ultrasonic imaging. It is possible that flow studies can help to identify those bypasses with suboptimal function, permitting the correction of kinking and improvement of run-off by extending the graft.

Summary

Flow measurements were made in 177 aortofemoral and 10 iliofemoral bypass limbs; the range of flow values did not differ between the graft types studied.

Flow showed correlation with symptoms and arterial run-off, and ankle pressure indices correlated with aortofemoral flow when the superficial femoral artery was patent.

Three bypasses in which poor blood flow had been recorded later failed. Causative factors were identified as severe diasease of the profunda femoris artery with poor run-off in two cases and kinking of one graft limb as it passed under the inguinal ligament.

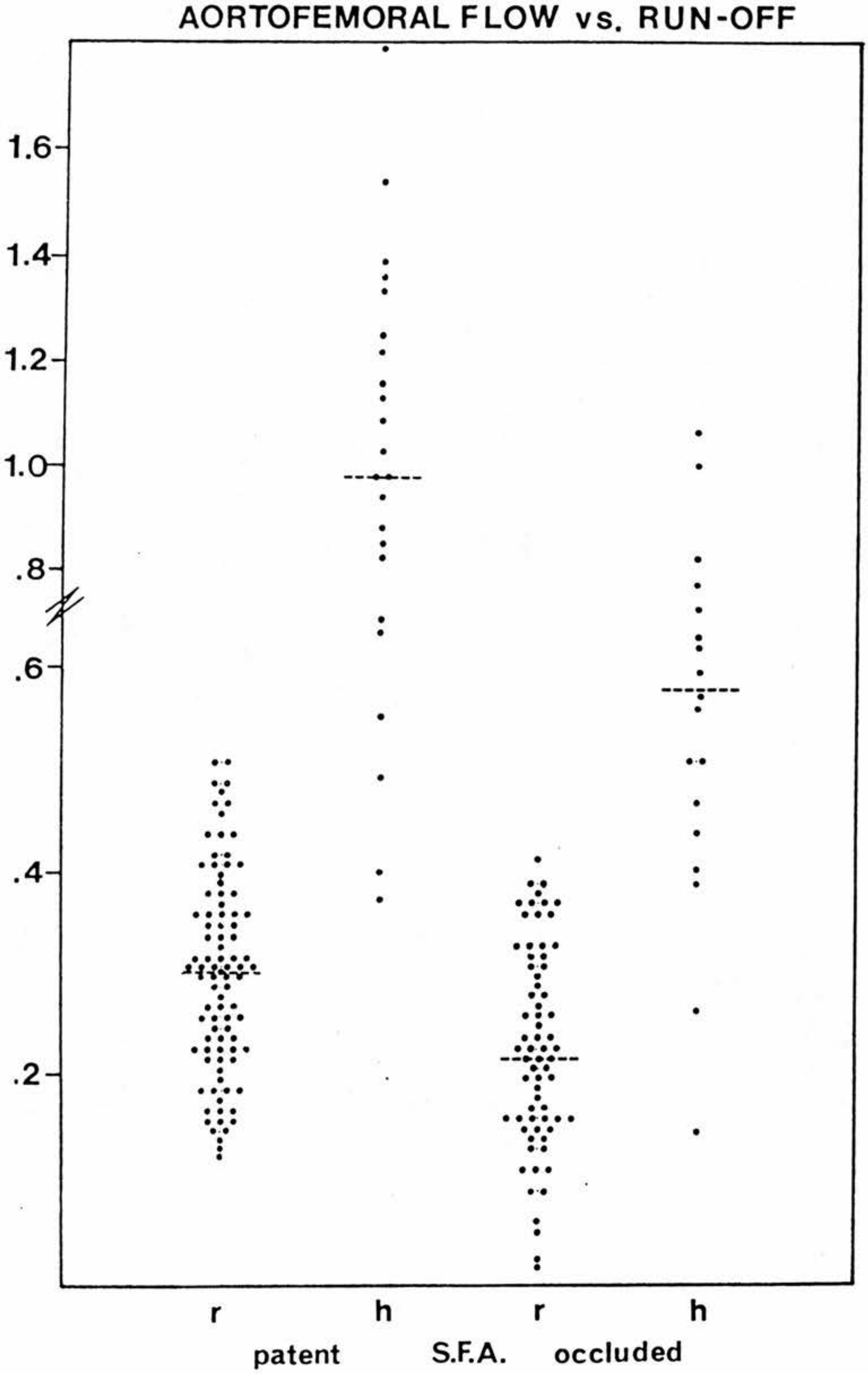


Figure 8.1: Resting (r) and peak hyperæmic (h) blood flow (l/min) in those aortofemoral bypasses for which a patent superficial femoral artery (S.F.A.) provided run-off compared with values for those in which this vessel was occluded. (*Note* there is a break in the linearity of the ordinate at 0.6 l/min).

Chapter Nine

A hæmodynamic evaluation of the femorofemoral cross-over bypass

Introduction

A crossover femoral to femoral graft seems first to have been used in 1951 by Oudot and Beaconsfield (1953) as a salvage procedure following occlusion of one limb of an aortobifemoral homograft. Freeman and Leeds (1952) reported a bypass from one common femoral artery to the other using a segment of endarterectomised superficial femoral artery, and McCaughan and Khan (1960) subsequently reported a similar technique. But the femorofemoral cross-over bypass was popularised chiefly by Vetto (1962) who reported 10 cases with only one early failure and follow up for 16 months, and proposed it as a "lesser operation that may be used effectively to relieve unilateral iliac artery obstruction in poor-risk patients". He subsequently (Vetto, 1966) reported good results in 32 of 38 cases.

Although initially confined to the correction of complications of previous aortofemoral reconstructions, Alpert *et al* (1967) recommended its use for the primary reconstruction of poor risk patients. Subsequently, its use was extended to primary reconstructions in suitable patients whatever their risk status (Jepson *et al*, 1970; Mannick, 1971; Baker and Parker, 1972). Not only were patency rates for femorofemoral grafts comparable with those for aortofemoral grafts (Parsonnet *et al*, 1970; Davis *et al*, 1972; Sethie *et al*, 1975), but the procedure was less traumatic, and there was less likelihood of disturbance of sexual function following pelvic dissection.

The femorofemoral cross-over bypass thus became a popular choice for the management of unilateral iliac artery disease, being used in preference to aortofemoral or extraperitoneal iliofemoral bypasses. It is a relatively minor procedure and is associated with few side effects. There is a small but definite risk of producing symptoms in the donor limb. This may result from operative damage to the donor artery or from the steal of blood from the donor limb by the bypass. Although this problem has been widely discussed, hæmodynamic studies have been limited by the use of indirect measurements of blood flow, such as ankle systolic pressures (Flanagan *et al*, 1978; Harris *et al*, 1981; Hines and Rivera, 1984; Todd *et al*, 1985), or by the use of electromagnetic flowmetry at the time of surgery (Graham *et al*, 1983).

With aims of studying the hæmodynamic effects of a femorofemoral cross-over bypass on the circulation in both the recipient and donor limbs, and of identifying preoperatively, problems likely to lead to hæmodynamic problems or to graft failure, the present study of 31 patients undergoing femorofemoral bypass was undertaken.

Patients and Methods

Thirty one patients (28 men and 3 women) aged 64 [40-79] years (median + range) were studied before and after insertion of a femorofemoral cross-over bypass for rest pain (n=18) or intermittent claudication (n=13). Preoperatively, all patients underwent uniplanar arteriography, and a non-invasive assessment of the blood flow to both limbs, consisting of A.B.P.I. following a standard two-minute exercise test, femoral pulse volume recordings (P.V.R.)(Raines *et al.*, 1976), femoral artery pulsatility indices (P.I.)(Gosling *et al.*, 1971) and Laplace δ (Skidmore and Woodcock, 1980).

At 3 [1-8] months postoperatively, patients were assessed clinically and examined again in the Vascular Studies Laboratory by post-exercise A.B.P.I. and blood flow measurements using the Technicare duplex scanner. Flow measurements were made at rest in the bypass and from the common femoral artery of the donor limb downstream from the origin of the bypass graft. Enhanced blood flow was produced in the bypass using a standard reactive hyperaemic test in which a pneumatic cuff was placed above the knee of the grafted (recipient) limb, inflated to 50 mm above systolic blood pressure for 3 minutes. Measurements of blood flow were made in the bypass within 20 seconds of the release of the occluding cuff, and then at 30 seconds after, in order to determine the peak postocclusion hyperæmic blood flow.

In order to examine the possibility that during hyperæmia the bypass might steal blood from the donor limb, a second hyperæmic experiment was performed. In this experiment enhanced flow was induced in the recipient limb as before, but flow measurements were made in the donor side common or superficial femoral artery beyond the bypass origin on release of the occluding cuff, and were repeated every 30 seconds throughout the duration of the contralateral hyperæmia.

Results

Clinical

All 31 patients reported some subjective improvement following surgery. In 29 cases there was either a complete abolition of symptoms or a very substantial improvement. In 5 cases, however, intermittent claudication was reported in the previously asymptomatic donor limb. In 3 of these, the onset of this symptom immediately followed surgery, and in 1 case was severely incapacitating.

Blood Flow

Resting blood flow in the bypass grafts was 161 [65-282] ml/min, increasing by 116% [5-428%] to 300 [82-1114] ml/min after hyperæmic testing (figure 9.1). Simultaneously, bypass hyperaemia caused a 32% [0-74%] fall in donor side femoral artery flow (figure 9.2).

Ankle Pressures

Postexercise ankle pressure ratios rose, in the operated limbs, from 0.31 [0.13-0.61] to 0.68 [0.32-0.92] postoperatively. Ankle pressure ratios fell in donor limbs from 0.94 [0.48-1.3] to 0.64 [0.14-1.3].

Steal related to preoperative assessment

Radiological evidence of significant occlusive disease (>50% luminal stenosis) affecting the donor iliac artery was present in 8 cases, and of less major disease in a further 6. Gruntzig balloon dilatation of the stenosis was carried out preoperatively in 5 of those with a major stenosis, with abolition of the pressure gradient in 4. In the other 3 cases the operation was performed for limb salvage in elderly patients. In all 10 cases with an uncorrected stenosis the donor limb steal, as measured by change in blood flow with contralateral hyperæmia, (48% [0-74%]), was significantly greater than in the 21 without evidence of a stenosis (15%[0-42%]; $p<0.001$, Mann Whitney U test) (figure 9.2).

There was no difference in preoperative donor femoral artery P.V.R. amplitude, P.I. or Laplace δ, either between those with and those without significant evidence of steal (>20% fall in donor blood flow), or between those who did or did not develop donor limb symptoms postoperatively. Although femoral pulse upstroke time was significantly longer in those patients who subsequently developed a >25% fall in donor blood flow during recipient limb hyperæmia, (240 [180-340] msec versus 210 [160-300] msec; $p<0.05$, Mann Whitney U test), there was no clear separation of values, nor a critical level of pulse rise time above which problems might be anticipated.

Symptomatic steal

Of the 5 patients who complained of donor limb symptoms postoperatively, only in 3 were these considered likely to be due to vascular steal, rather than to the unmasking of previously occult donor side arterial disease. Although in 2 of these 3 the resting ankle pressure ratio was virtually unchanged by the operation, in all 3 there was a marked fall in postexercise ankle pressure ratios (1.1, falling to 0.74; 1.2, falling to 0.70; 0.71, falling to 0.14). All 3 had had radiological evidence of donor iliac artery disease preoperatively. In one case, Gruntzig dilatation had failed to reduce the aortofemoral pressure gradient below 30 mm Hg. In a second case the stenosis, about 25%, was judged not likely to produce a hæmodynamic effect. In the third case, where the operation was carried out for rest pain in a poor risk, elderly patient, the abnormality was left untreated. All 3 had shown prolonged donor femoral artery upstroke time (240, 256, 270 msec), although these were not significantly different from the group of patients who were found to have a measureable but asymptomatic donor limb steal. Similarly, the other preoperative non-invasive parameters of donor iliac artery function would not have allowed identification of this group preoperatively.

Comparison with iliofemoral bypass

Although not suitable for all cases, the extraperitoneal iliofemoral bypass, from a patent or endarterectomised iliac artery, provides an alternative to the cross-over bypass for the management of a patient with unilateral iliac artery disease. The results of studies upon 10 such patients treated by iliofemoral bypass were described in Chapter Eight. Both operations produced a comparable and satisfactory improvement in stressed ankle pressure index (see page 113). Iliofemoral blood flow, both at rest and during hyperæmic testing was significantly greater (rest: 238 [133-413] ml/min versus 161 [65-282] ml/min, p=0.008, Mann Whitney; peak hyperæmic flow: 590 [173-1053] ml/min versus 300 [82-1114] ml/min, p<0.001, Mann Whitney).

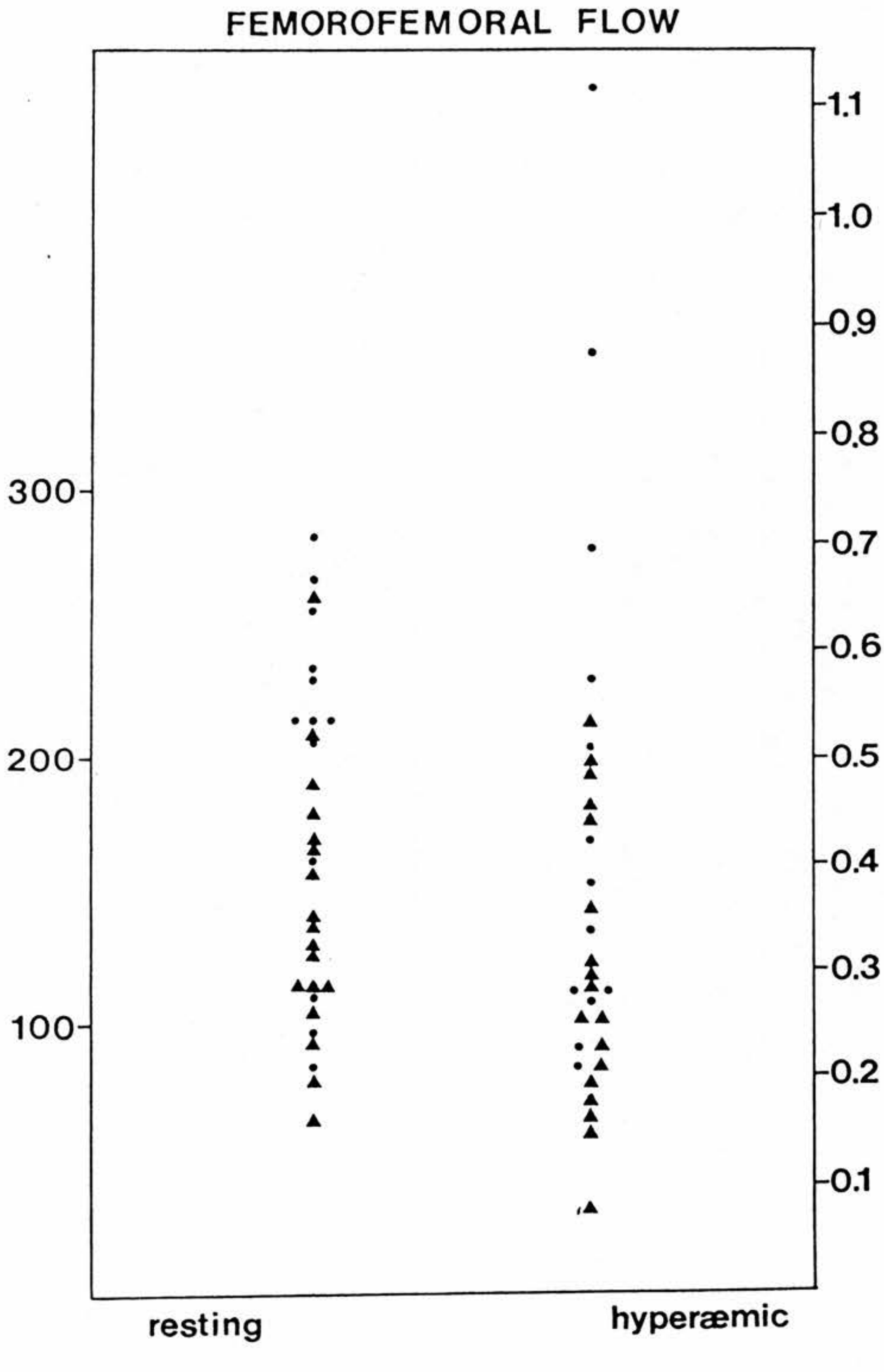


Figure 9.1: Resting and hyperæmic blood flow in femorofemoral bypasses.
The values for resting flow are given in ml/min by the right ordinate and for hyperæmic flow, in l/min, by the left ordinate. Those cases in which the operation was carried out for limb salvage are indicated by ▲, and by • in those bypasses for intermittent claudication alone.

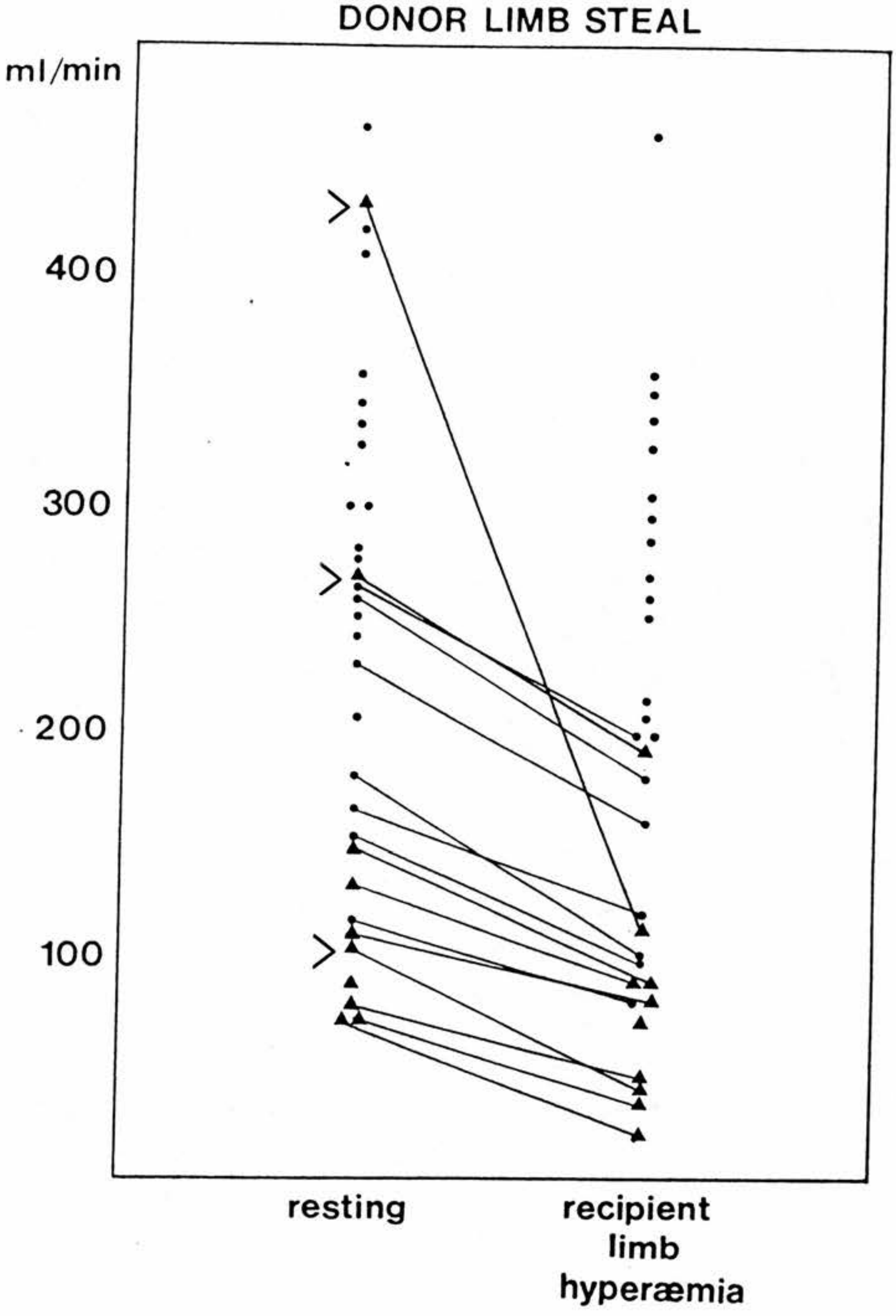


Figure 9.2: Blood flow measured in the the donor limb downstream from the bypass origin at rest and during peak hyperæmia in the recipient limb. In those cases in which a ≥25% steal of blood flow occured the paired flow values are linked by a continuous line.
> indicates those 3 cases in which the steal produced symptoms. The presence of radiologically apparent donor arterial disease is indicated by ▲.

Discussion

This study demonstrates that femorofemoral cross-over bypass has been successful in the management of patients with occlusive disease predominantly of one iliac artery, producing subjective and objective evidence of improvement in the majority of cases. Although stress testing produced evidence of donor limb steal in the majority, in only three of the 31 patients studied did this give rise to troublesome symptoms.

Extra-anatomical bypass is undoubtedly of value where an orthotopic procedure is not practicable. For instance, in circumstances where an infected septic field has to be avoided, or in the salvage of a bifurcated graft of which one limb has occluded. In addition, for debilitated patients of advanced age or limited life expectancy, a lesser procedure, either a cross-over or an extraperitoneal iliofemoral bypass, remains the operation of choice for localised occlusive disease of the iliac artery which is not amenable to balloon angioplasty. Truly unilateral iliac disease is infrequent, of course, and aortoiliac occlusive disease generally assumes a more diffuse and often bilateral distribution. DeBakey, in 1970, questioned the trend towards more widespread use of femorofemoral bypass for unilateral iliac disease because he feared progression of disease in the donor artery would result in premature graft failure. Indeed, progression of disease in the aorta or untreated iliac artery necessitated reoperation in a significant number of patients whose apparently localised disease had been treated by unilateral surgery (Crawford *et al*, 1975; Livesay *et al*, 1979).

Should the operation be regarded, therefore, as the primary treatment of choice for younger, good risk patients with unilateral iliac artery disease? Although patency rates are high, they are not as good as those reported with direct reconstruction if run-off and other factors are considered. Moreover, the present study demonstrates that both resting and hyperæmic blood flow to be significantly less good than for aortofemoral or iliofemoral bypass. In addition, there is a risk of developing a steal from the donor limb. Although not suitable for all cases, an iliofemoral graft, offers hæmodynamic advantages over the cross-over bypass, and may well be the preferred procedure.

Despite experimental evidence to suggest that it should not occur (Ehrenfelt *et al*, 1968; Shin and Chawdhry, 1979), the issue of donor limb steal has refused to go away since the early days of cross-over bypass (Warren and Fomon, 1966; Foley *et al*, 1969; Trimble *et al*, 1972; Sumner and Strandness, 1972). The fact that the diagnosis has been made solely on clinical grounds or on indirect hæmodynamic evidence, for example ankle pressure changes alone, has not helped to clarify the situation.

In the present study, most of the cases with objective evidence of an asymptomatic steal had been elderly, more sedentary patients with critical ischæmia. Harris *et al* (1981) found a worsened exercise tolerance as assessed by postexercise ankle pressures in the donor limb of 20 of 44 patients treated by femorofemoral graft for intermittent claudication, and suggested that, in claudicants, there is flow diversion from the donor limb during exercise in a significant number of patients, even though this may not cause symptoms. In the present study, 2 of the 3 who developed clinical symptoms of steal had been relatively young and active claudicants,

The development of donor limb symptoms postoperatively does not of itself, of course, prove that a vascular steal is the cause. Abolition of a more severe contralateral claudication or rest pain may unmask a previously unrecognised arterial insufficiency in the donor limb. Alternatively, a carelessly applied clamp may damage the donor limb femoral artery resulting in the development of new symptoms postoperatively. Only if a steal can be demonstrated hæmodynamically and the donor limb shown to function satisfactorily when stress tested independently of the grafted limb, can symptoms of ischæmia in donor limbs be attributed to a vascular steal by the cross-over bypass.

The findings of the present study are in accordance with those of Flanagan *et al* (1978), who claimed evidence of vascular steal in 80% of their patients with cross-over grafts, but found this was rarely of clinical significance. The steal was worse if donor side occlusive disease were present upstream or downstream of the bypass origin. Indeed, the importance of donor iliac stenosis in the development of steal and of premature graft failure has long been recognised (Vetto, 1962; Sumner and Strandness, 1972), and has been borne out by the present findings.

The apparent inability of the non-invasive tests to correlate, either independently or in combination, with the degree of steal as measured, ultrasonically by a fall in donor side flow, is disappointing. Although arteriographs have best shown the presence of donor iliac artery disease, the problems of equating uniplanar radiographic images with hæmodynamic function are well recognised. Radiographs in at least 2 planes would yield more reliable information, as would direct pressure measurements of pressure gradients across the donor aortoiliofemoral segments.

Summary

The femorofemoral cross-over bypass is ideally suited for study using duplex ultrasound. The whole length of the bypass is easily imaged, and its relatively superficial position makes Doppler sampling easy and reliable. Although resting and hyperæmic flows were generally satisfactory, the values were significantly less than those measured in patients with aortofemoral or iliofemoral bypasses.

Flow measurements in the donor limb during selective reactive hyperæmia of the recipient limb showed some evidence of donor limb steal. However, this only gave rise to troublesome symptoms in 3 of the 31 patients studied.

The development of steal was most noticeable where there was radiological evidence of donor iliac artery disease. A prolonged upstroke time in the donor femoral artery P.V.R. was the most accurate non-invasive predictive test.

Abolition of a donor artery pressure gradient by balloon angioplasty was an effective pre-or peroperative adjunct to a cross-over bypass.

Chapter Ten

Carotid blood flow

Introduction

The aims of the present study were to identify the ranges of blood flow in normal carotid vessels under physiological conditions, and to relate changes in blood flow volume to radiologically identified disease of the internal carotid artery and to patients' symptoms. Improved blood flow following carotid endarterectomy was measured in the short term and was related to symptoms in order to attempt an explanation as to whether the clinical symptoms of carotid disease are invariably associated with reduced blood flow.

Patients and Methods

Both common and internal carotid arteries were studied in 59 subjects. In 37 internal carotid arteries, stenoses were identified using duplex ultrasound and these were all further quantified using triplanar arteriography. At least 4 estimates of blood flow were made from each artery for the measurements "at rest", using a Technicare Autosector duplex scanner, and the average taken. All patients were studied in a seated position following a 10 minute rest period.

The common carotid artery was identified sufficiently well in all patients for reproducible diameter measurements and flow measurements to be obtained from it. For the internal carotid artery, flow measurement depended upon the visualisation of of an adequate length of artery from which acceptable flow signals could be obtained using an ultrasonic beam inclined with the blood vessel at a sufficiently acute angle ($\leqslant 55^{\circ}$). In 115 of the 118 internal carotid arteries (97.5%), acceptable flow signals were obtained. The carotid bifurcation in one case lay so high that no reliable flow values be obtained from the internal carotid arteries. In one patient with a major stenosis of the internal carotid artery, flow signals were so distorted by the turbulent movement of blood through this vessel that accurate flow measurement was not possible.

In 6 of the normal healthy volunteers, the internal carotid artery blood flow was measured at rest and following a vigorous exercise test (15 minutes of walking at 6km/hr on a treadmill). In the same subjects, the effects of hypercapnia and hypocapnia were studied following rebreathing into a polythene bag for 2 minutes and by forced hyperventilation for 1 minute. In all cases, flow measurements were repeated every 15 seconds until resting levels were reached.

Fifteen patients undergoing carotid endarterectomy were studied. Of these, 14 had a stenosis of the internal carotid artery of at least 75% luminal reduction, as assessed both by ultrasonic scanning and by triplanar contrast radiography. The remaining patient had an ulcerated atheromatous plaque with a 30% stenosis. Blood flow measurements were made within a few days preoperatively and again at 1 month postoperatively. Healing tissues made transcutaneous flowmetry difficult and unreliable in the immediate postoperative period.

Results

Resting flow values for common and internal carotid arteries, according to the degree of internal carotid stenosis, are set out in table 10.1.

Table 10.1

degree of stenosis	*common carotid flow*	*internal carotid flow*
normal (n=81)	420 [258-697] ml/min	276 [172-411] ml/min
<50% (n=12)	449 [304-537] ml/min	289 [189-392] ml/min
50%-75% (n=6)	391 [305-459] ml/min	242 [146-341] ml/min
>75% (n=17)	339 [131-460] ml/min	185 [46-243] ml/min
occluded (n=2)	51 [39- 63] ml/min	0 ml/min

Blood flow was significantly reduced by a >75% stenosis ($p \ll 0.001$, Mann Whitney), but not by lesser degrees of luminal narrowing (table 10.1, figures 10.1 and 10.2).

In normal arteries, there was no significant diffence in flow values between the male and female sujects, nor were there any age-related differences. For patients with a >75% stenosis enhanced flow was found in the contralateral internal carotid artery, except where occluded, (301 [214-379] mls/min ($p<0.02$, Mann Whitney U test) irrespective of the degree of any stenosis; the ratio of the contralateral flow to that in the more severely stenosed vessel was 1.60 [0.87 to 8.24] ($p<0.0001$, Mann Whitney).

Physiological Changes (figure 10.3)

Hypercapnia induced by rebreathing caused a rise in internal carotid blood flow to 186% [154-219%] of the resting levels. Recovery was rapid and resting levels of blood flow were reached within 30 seconds.

Hyperventilation produced an expected fall in the internal carotid flow to 57% [49-71%] of the resting value. In all 6 cases, resting levels ±15% were reached within 30 seconds of the end of the hyperventilation.

Although the exercise test produced an 80% [60-115%] rise in pulse rate in the 6 normal volunteers, the internal carotid after the test in no case varied by more than 15% from the resting level (105% [94-114%]).

Endarterectomy (figure 10.4)

In 15 patients studied who underwent endarterectomy, blood flow in the common carotid of the affected side increased from 335 [131-426] to 436 [130-517] ml/min, and in the diseased internal carotid from 188 [46-263] to 322 [63-423] ml/min. In all 15 patients, symptoms were entirely abolished by surgery, and all have remained well when reviewed one year postoperatively.

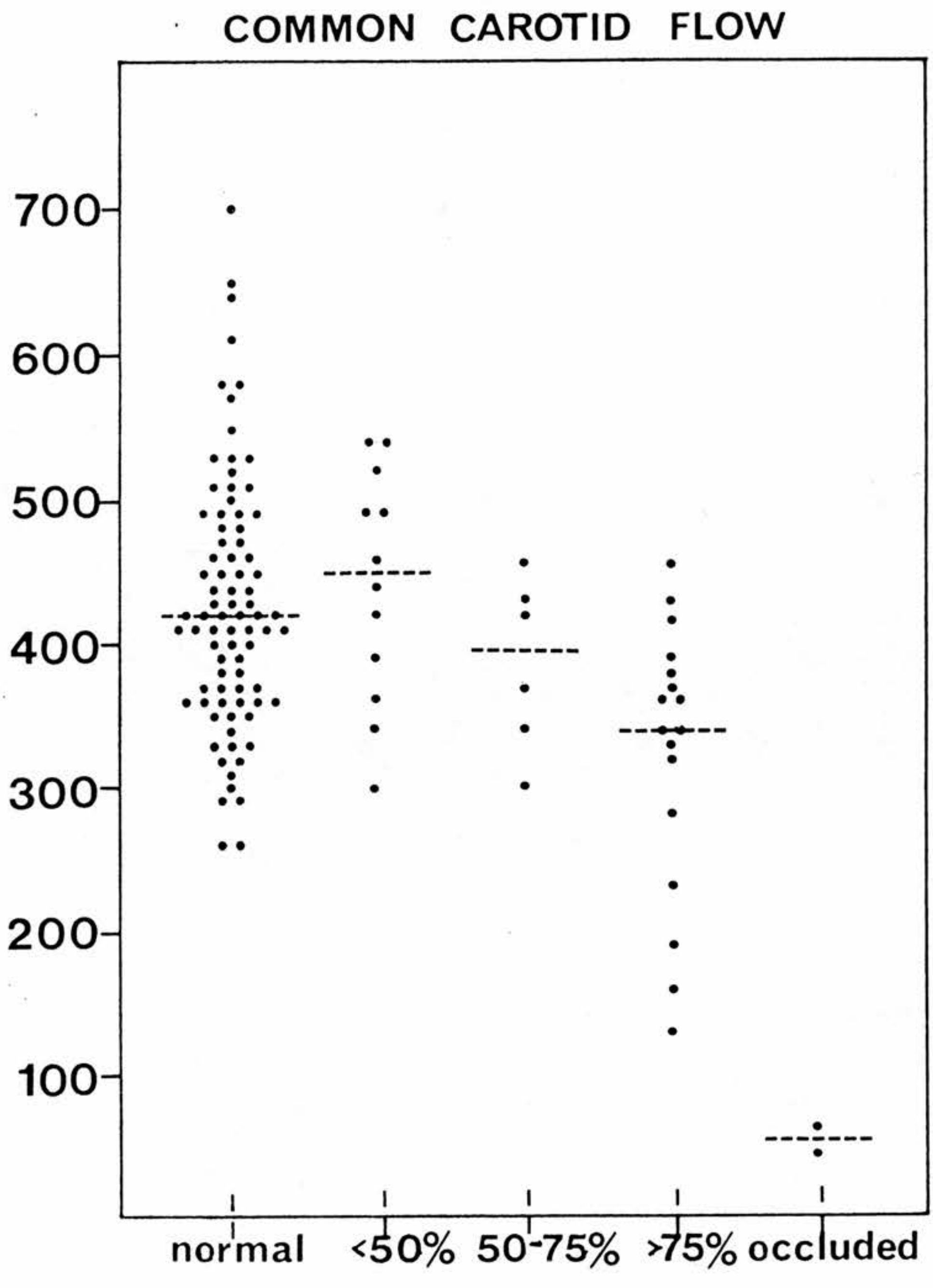


Figure 10.1: Resting blood flow values (ml/min) in the common carotid arteries according to the state of the internal carotid artery as assessed by duplex ultrasound and, in 37 cases, by triplanar radiology.

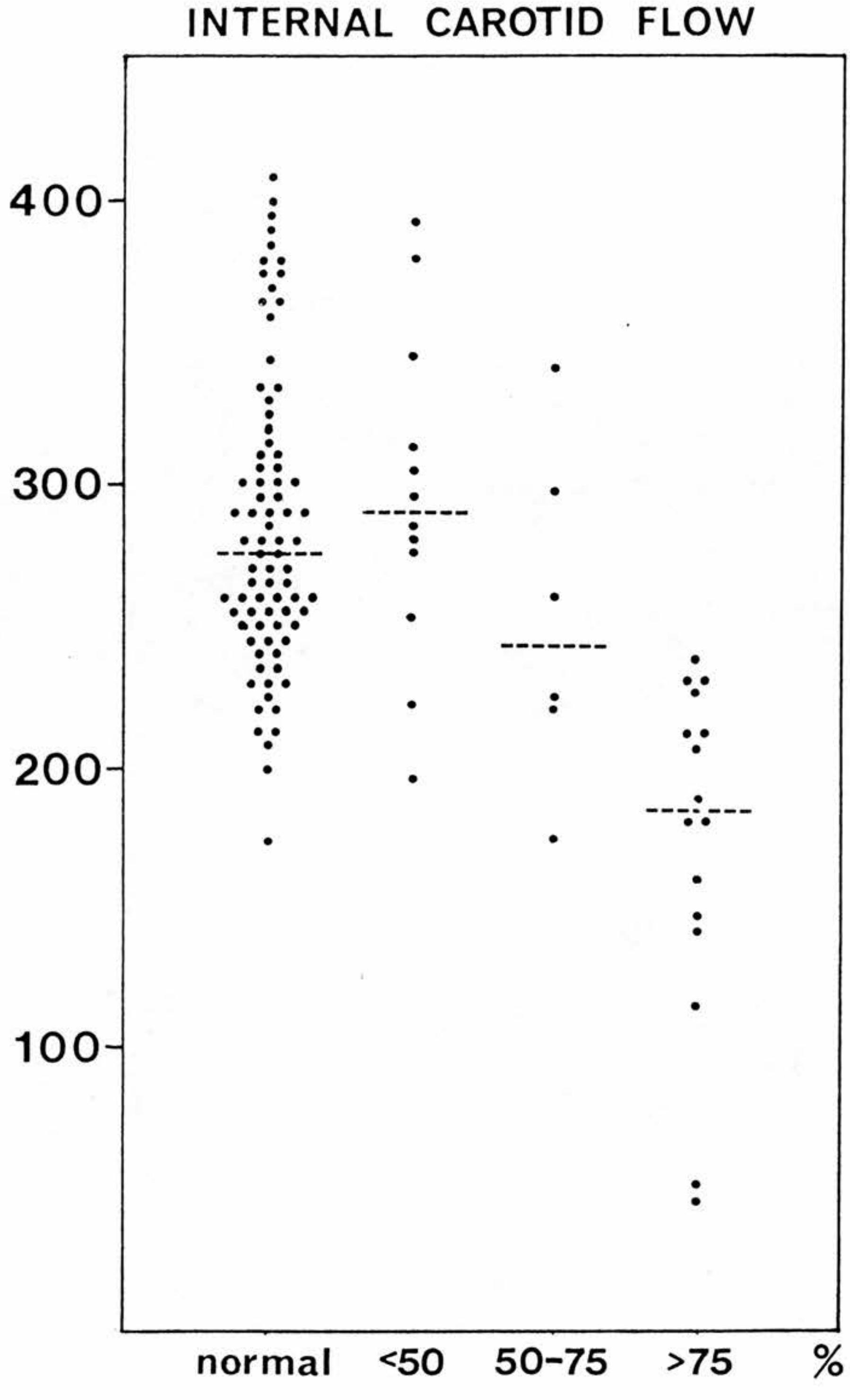


Figure 10.2: Resting blood flow values (ml/min) in the internal carotid arteries, according to the degree of stenosis of each vessel assessed ultrasonically and, in 37 cases, by triplanar radiology.

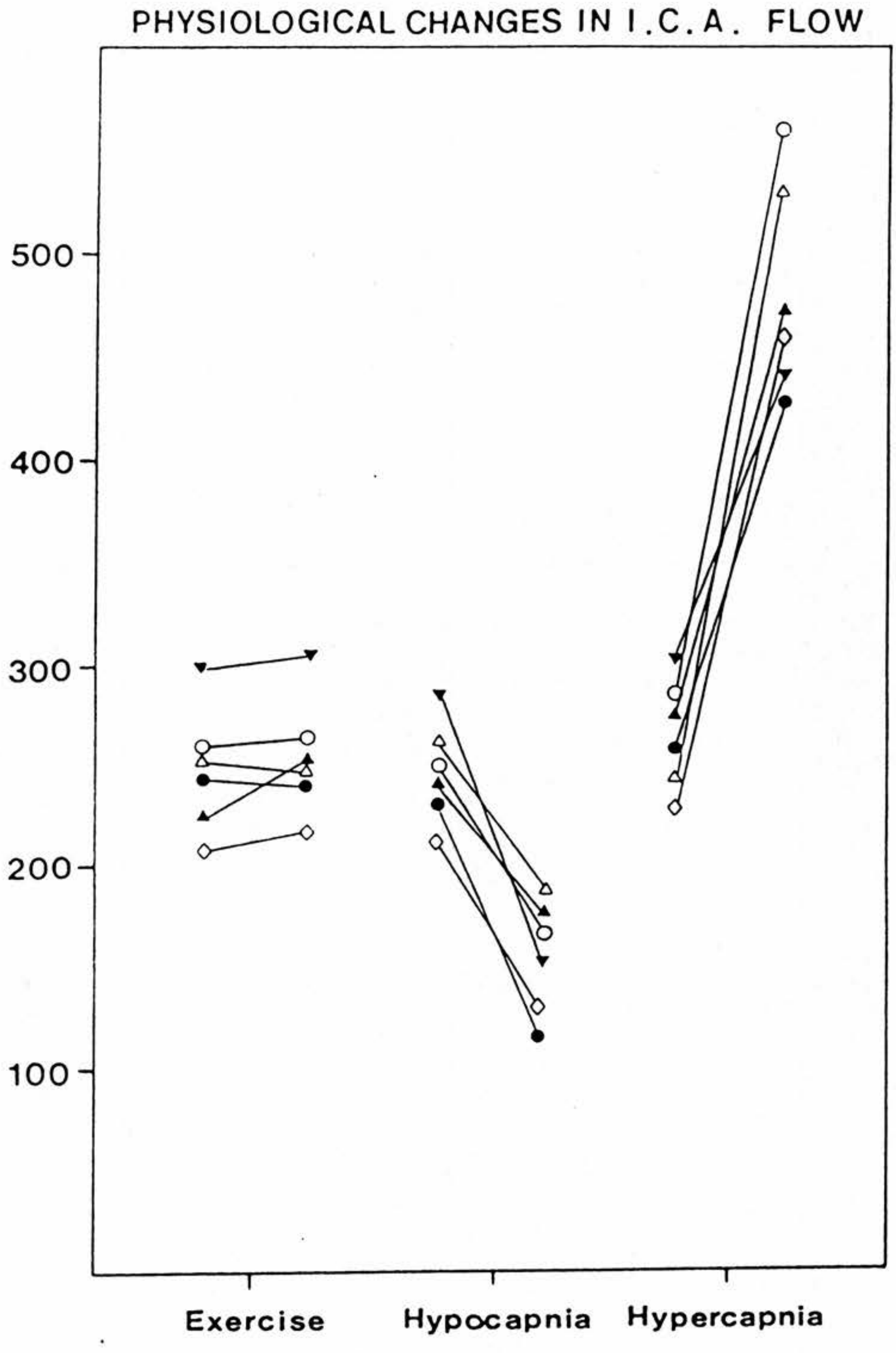


Figure 10.3: The effects of exercise, hypercapnia, induced by rebreathing, and hypocapnia, induced by forced hyperventilation, on internal carotid blood flow (ml/min) in 6 normal subjects.

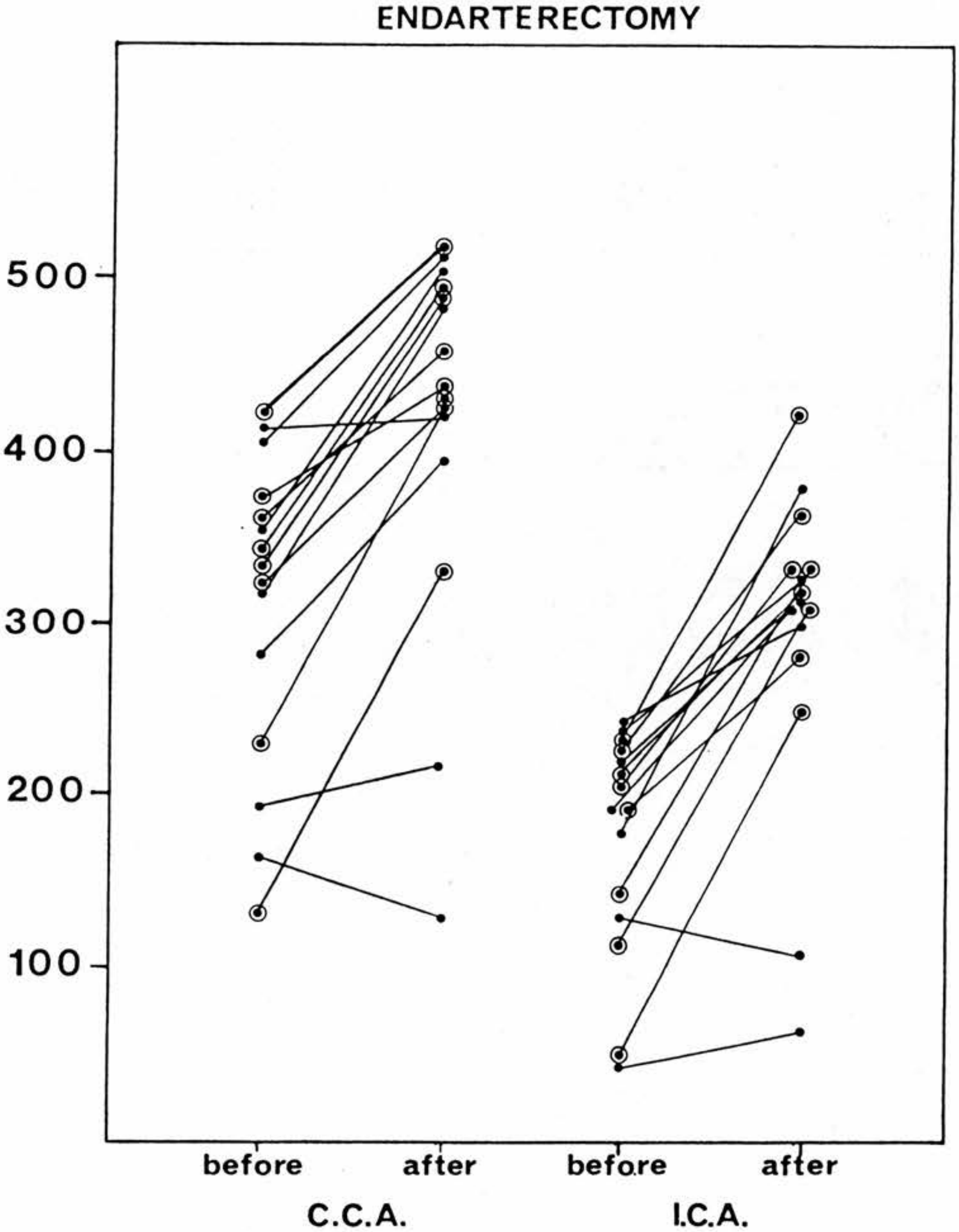


Figure 10.4: Resting blood flow (ml/min) in the common carotid (C.C.A.) and internal carotid (I.C.A.) arteries, measured before and after endarterectomy for symptomatic disease of the internal carotid artery. Those arteries with a preoperative stump pressure of ≤50mm Hg are indicated by ⊙.

Table 10.2

Carotid blood flow

Author	Method	n=	Internal carotid	Common carotid
Kristiansen,Krog 1962	e/m	5	350	500
Cappelan,Hall 1963	e/m			
Roberts *et al* 1964	e/m	11	370	-
Cordell *et al* 1968	e/m	>10	239	370
Borodzinsky *et al* 1976	Range gated pulsed Doppler		-	530
Keller *et al* 1976	Range gated pulsed Doppler¶	22	-	300-480
Mizukami *et al* 1981	Range gated pulsed Doppler	29		490±143
Payen *et al* 1982	Range gated pulsed Doppler		-	387±183
Fitzgerald *et al* 1982	Range gated pulsed Doppler	25	-	526±104
Uematsu *et al* 1983	Doppler ultrasound†		-	[360-660]
Benetos *et al* 1985	Doppler Ultrasound	24	-	380 [250-520]
Lee (1987) present study	Duplex ultrasound	81	276 [172-411]	420 [258-697]

e/m = electromagnetic flowmetry

¶ = semi-quantitative only

† = phase-locked A-mode ultrasound for location and measurement of blood vessel diameter

Published values for blood flow (ml/min) (mean ± S.D. or median + range) measured in internal and common carotid arteries.

Discussion

Resting blood flow

Kety and Schmidt, in 1946, first measured cerebral blood flow in healthy men using a nitrous oxide washout technique. Their mean value of 54 ml/100mg/min represents about 750 ml/min, corresponding with a flow in each internal carotid artery of 200-300 ml/min.

With the advent of the electromagnetic flow probe, measurements of blood flow in intact individual blood vessels became feasible. Measurements of blood flow in exposed carotid vessels were made in patients undergoing surgical operations upon the neck, including carotid endarterectomy. Values reported range widely from 325-500 ml/min for the common carotid and 239-370 ml/min for the internal (table 10.2). External carotid flow in man was found to be 54-60% of that in the internal carotid. Samnegård and Elekström (1974) recorded internal carotid blood flow measurements for up to 5 days following carotid endarterectomy using an electromagnetic flowmeter implanted at the time of surgery. Since then, quantitative measurements of flow in individual vessels in conscious subjects have all used ultrasonic methods.

Keller *et al* (1976) reported flow values of 300-480 ml/min using ultrasound, but their results are flawed by the absence of measurements of the angle of incidence of the ultrasound beam to the blood vessel. Borodzinsky *et al* (1976), Payen *et al* (1982) and others used range gated ultrasonic flowmetry to study carotid blood flow, obtaining values of 380-530 ml/min for blood flow in the common carotid (table 10.2). This technique, whereby the instantaneous average velocity of blood flow is calculated at various points across the blood vessel diameter, is based upon the assumption that the blood vessels and blood flow elements are circularly symmetrical. Uematsu *et al* (1983), using a Doppler system incorporating a phase-locked A-mode echo-tracking method for measuring the common carotid artery diameter and a fixed angle ultrasonic velocimeter, measured common carotid blood flow in health and in a number of pathological states.

The duplex scanner represents an advance over other ultrasonic methods in that volume flow measurements then supplement measurements of grades of stenosis (Theile *et al*, 1980) and the study of the morphology of atheromatous plaques (Reilly *et al*, 1983), which are available using this equipment. Moreover, the use of ultrasound for the measurement of flow in the internal carotid requires that this vessel be adequately identified; the variable position of the carotid bifurcation and the disposition of the internal and external carotid vessels above it would make flow measurement without an adequate imaging facility difficult and unreliable. Fixed angle flowmeters, like the range gated Doppler, cannot reliably measure flow in deep seated or curved vessels For this reason, none of the authors cited earlier have reported internal carotid artery flow measurements, although this is surely the vessel of greatest interest. In the present study, acceptable flow measurements were obtained in some 115 of the 118 internal carotid arteries studied.

<u>Relationship of blood flow to stenosis</u>

A diameter stenosis of $\geq$75% or complete occlusion of the internal carotid artery was needed before blood flow in the common or internal carotid arteries was significantly reduced. This is in accordance with the widely held view that a major stenosis of $\geq$80% is required before the mean blood flow is reduced (May *et al*, 1963; Weale, 1964), and has been described in the carotid circulation by several other authors, including Benetos *et al* (1985). Fitzgerald *et al* (1982), in their large series of 550 common carotid arteries, found that, although there was a relationship between flow and the degree of stenosis, the correlation was better for those groups with very mild and very severe stenoses. Similarly, Uematsu *et al* (1983) describe a significant inverse linear relationship between flow and degree of stenosis.

In those patients with a $\geq$75% stenosis of one internal carotid, flow in the contralateral artery was found to be enhanced, provided this vessel was patent. Roberts *et al* (1964), using electromagnetic flowmetry to study flow in internal carotid and vertebral arteries, found that sudden occlusion of 1 of the 4 vessels caused an immediate compensatory rise in blood flow in the remaining 3. A similar observation was made by Kristiansen and Krog (1962), who demonstrated an increase in common carotid flow by compressing the contralateral carotid. Contrary to the present study, Benetos *et al* (1985) did not find that a stenosis of one carotid produced augmented flow in the opposite common carotid in the long term.

Relationship of blood flow and $PaCO_2$

Hypercapnia produces augmentation of the internal carotid blood flow. Such an increase in flow might disclose the hæmodynamic significance of a stenosis not seen with resting measurements.

Kety and Schmidt (1946) studied the effects of altered $PaCO_2$ and PaO_2 on the cerebral circulation of normal young men, using a N_2O washout technique. Although hyperventilatation produced no change in cerebral blood flow, they demonstrated an exponential relationship between $PaCO_2$ and cerebral blood flow. Elekström (1968) and Hayes and Tyndall (1969) demonstrated an increase in internal carotid blood flow with hypercapnia using electromagnetic flowmetry on anæsthetised subjects, and an exponential relationship was confirmed by Samnegård and Elekström (1974) in conscious post-endarterectomy patients. Uematsu *et al* (1983) found that hyperventilation produced a fall in common carotid blood flow of about 50%, whereas hypoventilation and exercise had no measureable effect on flow.

The alterations in $PaCO_2$, produced by hypo- and hyperventilation in the 6 normal subjects of the present study, were associated with transient changes in the internal carotid blood flow. The experiment was of the nature of a preliminary study to determine whether the blood flow changes produced by alterations in $PaCO_2$ were reproducible and easily measured. Enhanced carotid blood flow might then serve as a measure of the adequacy of carotid function, rather like the exercise or reactive hyperæmic stress used in the testing of lower limb circulation. Although the changes could easily be reproduced by similar stresses, the measurements were not easily made, because the duration of the alteration in blood flow was so brief, and the test required a high degree of cooperation and understanding from the subject being tested. It was felt that the technique would be insurmountably difficult to apply to patients, and further quantitative studies were not undertaken.

Blood flow and carotid endarterectomy

Some early reports suggested that there might be a relationship between clinical improvement after carotid endarterectomy and an increase in blood flow measured immediately after the operation (Cappelan and Hall, 1963), but later reports do not support this (Golding and Cannon, 1966; Samnegård and Elekström, 1974). In the present study, the increase in flow brought about by surgery was more pronounced in those patients in whom an internal carotid stumppressure <50 mm Hg was present. Cronestrand (1972) noted a greater increase in flow in those 36 patients who had a ≥5 mm Hg pressure gradient at operation compared with 34 in whom no gradient greater than 5 mm Hg was present. Elekström (1968) described a >20% increase in flow following endarterectomy in 26 out of 48 carotid arteries. of these 26, 18 had had a ≥10mmHg pressure gradient measured at operation. Only 1 other patient with a ≥10mmHg pressure gradient failed to achieve a ≥20% increase in flow postoperatively.

Samnegård and Elekström (1974) recorded internal carotid artery flow for up to 5 days following carotid endarterectomy by implanting a square wave electromagnetic flow probe at the time of surgery. The immediate post-reconstruction flow increased by 67% to a maximum at 24 hours postoperatively, falling thereafter to a level rather greater than the preoperative value. They found no difference between those patients with and those without a preoperative pressure gradient. As in other locations, it was difficult, using duplex ultrasound, to measure blood flow in the carotid arteries in the immediate postoperative period. Interference with surgical wounds and the difficulty in obtaining adequate images and flow signals through the healing tissues limits the use of ultrasonic flowmetry to a period after at least 1 week following surgery. In 3 of the 15 patients, endarterectomy did not increase the volume of blood flow despite abolition of symptoms. This finding lends support to the view that, in a few cases, symptoms arise from atheromatous plaques which do not produce a hæmodynamic effect. Removal of these lesions removes the source of symptoms, perhaps platelet microembolisation, without necessarily increasing blood flow.

Summary

Blood flow measurements were made in the common and internal carotid arteries of 59 patients and normal subjects. Measurements were easily obtained in the common carotid arteries, and in all but 3 internal carotids. A stenosis of >75% was required before blood flow was reduced below the normal range of values.

Hypercapnia produced measureable and reproducible augmentation of the internal carotid blood flow of 6 healthy subjects.

Endarterectomy produced an increase in flow in 12 of 15 patients. All patients were rendered asymptomatic, even those in whom the operation produced no increase in flow.

Chapter Eleven

Discussion

The major work of the thesis concerns the application of ultrasonic flowmetry to the follow-up of patients with arterial reconstructions; its feasibility and the usefulness of the flow measurements in the detection of a failing bypass and the prediction of occlusion.

Femoropopliteal reconstructions

Flow measurement in femoropopliteal bypasses was relatively straight forward. The bypass was easily accessible to the real-time echo ultrasound, and virtually the whole length of each bypass could be imaged in this way, permitting recognition of luminal irregularities. Flow signals were easily obtained, and the range of luminal size combined with the relatively superficial position of each bypass enabled accurate positioning of the pulsed Doppler beam to encompass the whole cross section. The flow values, except for a few abnormally functioning bypasses, lay within the optimal range for the flowmeter. Hyperæmic testing was well tolerated by the patients, who found the below knee occlusion cuff much less uncomfortable than the above knee position adopted in the studies of patients with more proximal reconstructions. The total examination time for a patient with a femoropopliteal bypass was 20 to 30 minutes. The high attrition rate of femoropopliteal bypass patency and the incidence of recurrent symptoms makes regular follow-up of this kind very much in the patient's interest.

A poor response to reactive hyperæmic testing is a well established method of identifying a failing femoropopliteal bypass and proved accurate in the prediction of occlusion. Blood flow and ankle pressure ratios measured at rest proved much less reliable, largely because of the very wide range of values for resting blood flow which were found in normally functioning bypasses. A deterioration in function of a failing bypass was better detected as a reduction in post-occlusion hyperæmia. A deterioration in the post-exercise A.B.P.I., was the most accurate single measure of a deteriorating bypass function. Certainly, the excellent correlation between A.B.P.I. and femoropopliteal bypass flow suggests that the ankle pressure ratio is an excellent index of the flow in the superficial femoral artery or its bypass equivalent.

Aortofemoral reconstructions

Imaging of the distal part of aortofemoral bypass limbs was easily made; the high resolution real-time system permitting a detailed examination of luminal characteristics and a study of the diameter changes of fabric grafts after implantation. Although the femoral anastomosis was easily visualised, some practice was required before accurate interpretation of the images could be made; in particular, the presence of a small anastomotic pseudoaneurysm was difficult to diagnose. Nevertheless, ultrasonic imaging probably offers the most reliable and acceptible method of studying bypass graft morphology, and particularly of the abnormally dilated graft. Unfortunately, the 7.5 MHz. head of the Technicare scanner did not provide sufficient penetration to examine the more proximal portions of aortofemoral bypasses. It would have been interesting to compare diameter changes in the graft limbs with those involving the trunk of the bifurcated prostheses. Flow measurements posed more technical problems than measurements in femoropopliteal bypasses since a more limited length of bypass lay within the focal range of the instrument It was found that the iliac section of the bypass limb, visualised by placing the ultrasonic transducer in the inguinal crease, provided a regular, straight length of bypass lumen which was ideally placed for an interception with the Doppler beam of about 50°. The wider lumen of the bypass limbs sometimes made it difficult to encompass the whole luminal cross section by the Doppler beam sample volume, whilst the close proximity of the iliac vein made it difficult to obtain clean flow signals in some cases. The examination and measurement of flow in aortofemoral bypasses certainly required more expertise than the corresponding examination in femoropopliteal bypass, and was more time consuming, sometimes both limbs taking over an hour.

An added difficulty proved to be the application of reactive hyperæmic testing to these patients. Much the best results were found using a proximal thigh occlusion cuff, but some patients found the inflated cuff too painful to tolerate for the prescribed 3 minutes, so hyperæmic flow values are incomplete for this group of patients. As the study progressed, it was found necessary to apply hyperæmic testing only to those patients with low flow values at rest or in whom symptoms, signs or other evidence of flow insufficiency were present. The relatively low incidence of problems following aortofemoral bypass grafting and the low rate of occlusion of such bypasses makes the regular follow-up of such patients more of a research interest than a service need.

Femorofemoral reconstructions

Femorofemoral bypasses, on the other hand, are highly amenable to study with duplex ultrasound. The entire bypass, including the anastomoses, is readily visualised and flow values are easily obtained. The phenomenon of arterial steal from the bypass limb, which has for so long been described and disputed, can be identified and quantified.

Diagnostic ultrasonics is a rapidly advancing technology, with developments bringing about increased ease of operation and improvements in machine performance. Such improvements are likely, in a relatively short time, to improve upon those aspects of the flowmetry technique which have given rise to errors and inaccuracies, such as the improvement of uniform insonification and the definition of the size of the sample volume of the pulsed Doppler beam. Improvements in the imaging facility may reduce operator error in the measurement of blood vessel diameter, and any facility which would improve upon the accuracy of measuring angle θ would be welcomed. The advent of ultrasound systems, currently being developed, which may calculate the volume blood flow independently of a measured angle θ, is awaited with interest. For the routine regular follow-up of patients with arterial reconstructions, the great deal of information which the duplex ultrasonic flowmeter can provide certainly makes this the preferred technique for the follow-up of femoropopliteal and "extra-anatomical" bypass grafts. Perhaps the relative simplicity with which the volume blood flow can be measured using this attractive ultrasonic technique may help clinicians think in terms of the volume flow in their assessment of the adequacy of the circulation.

Chapter Twelve

Summary and conclusions

Ultrasonic flowmetry, performed using a Technicare Autosector duplex scanner, was evaluated as a tool for diagnosis and in the follow-up of patients with arterial reconstructions.

In vitro experiments designed to test the accuracy of the system demonstrated a linear response to blood flow over the range 50-1000 ml/min. The angle subtended by the Doppler ultrasound beam with the flowing blood was critically important; errors were minimised by using as acute an angle of approach as possible that would permit complete interrogation of the blood vessel by the Doppler sample volume, generally between 45° and 55°. *In vivo* studies demonstrated that the technique produced acceptibly reproducible results.

The normal values for resting blood flow in the femoral arteries were established by measurements in a group of normal, asymptomatic subjects. The values, 337±64 ml/min for the common femoral artery and 202±57 ml/min for the superficial femoral (mean± standard deviation), were taken to represent ideals for postoperative flow rates in aortofemoral and femoropopliteal reconstructions. These values are noticeably higher than those measured in anæsthetised patients using electromagnetic flowmetry, but are comparable with flow measured in conscious patients using other techniques (table 4.2)

The need for stress testing was met by using a post-occlusion hyperæmic test. Reactive hyperæmia following a 3 minute period of circulatory arrest was found to be most suitable, producing a hyperæmia comparable with that following 2 minutes of treadmill exercise. The hyperæmic response enabled the normal subjects to be separated from claudicants with a superficial femoral artery occlusion and those with disease predominantly of the iliac artery.

Real-time ultrasound was used to study morphological changes in implanted bypasses. In vein grafts, regions of dilatation and stenosis were easily identified and vein valve remnants were seen in *in situ* bypasses. In most cases these were flimsy and mobile, and in a few the cusps had become fixed and fibrosed. In two veins, stenosing lesions were identified. In knitted Dacron bypass a tendency towards dilatation was seen, which was more pronounced in double-velour grafts and did not seem to be related to time from insertion. Aneurysmal dilatation was observed in 3 double-velour knitted Dacron grafts, all inserted in hypertensive patients for more than 4 years. Anastomotic false aneurysms were found in 3 patients. In woven Dacron grafts, the bypass diameter was reduced by tissue encroachment upon the lumen

Ultrasonic flowmetry was used to study and for routine follow-up of 85 femoropopliteal bypasses. Flow values showed good correlation with symptoms and with ankle systolic pressure indices, especially when the hyperæmic flow was considered. Flow values were closely related to the extent of the run-off as demonstrated by preoperative arteriography. A poor hyperæmic response was the best index of a failing bypass. A fall in the post-exercise A.B.P.I. and a deterioration in the hyperæmic response between six-monthly examinations predicted graft occlusion most accurately. Resting blood flow, resting ankle pressures and clinical symptoms and signs were not good indices of graft function. Five bypasses identified by non-invasive criteria as being in danger of imminent occlusion were investigated by arteriography, and successful salvage surgery was carried out in 2. Six bypasses occluded unexpected. In these cases, 4 of which were of fabric material, occlusion was presumed to be the result of a sudden thrombosis, perhaps related to kinking of the bypass at the level of the knee joint, which was crossed by all the grafts.

In 177 aortofemoral bypass limbs, blood flow measurements correlated with symptoms and with arterial run-off. The correlation with ankle pressure ratio was poor when the superficial femoral artery was occluded, suggesting that, although they are a good index of superficial femoral artery or femoropopliteal bypass flow, the presence of concomitant distal arterial disease may make ankle pressure ratios a poor index of aortofemoral bypass flow. Two bypasses occluded during the study; both had shown very poor blood flow both at rest and during reactive hyperæmia; real-time imaging had demonstrated that the lumen of one was narrowed by kinking at the inguinal ligament. The only difficulty proved to be the measurement of hyperæmic blood flow, as some patients found a high thigh occlusion cuff difficult to tolerate for a full 3 minutes

In 31 femorofemoral cross-over bypasses, blood flow was found to be significantly less, both at rest and during hyperæmia, than in patients with comparable disease who had undergone aortofemoral or iliofemoral reconstruction. A hæmodynamic experiment was carried out in order to unmask any steal of blood from the donor limb by the bypass, and to quantify this. Although some evidence of steal was present in the majority of patients, in only 3 was this of a degree which would be significant clinically. Radiological evidence of disease affecting the donor iliac artery was significantly related to the subsequent development of steal, although none of the non-invasive tests carried out preoperatively proved effective in identifying those bypasses at risk of the development of donor limb steal. Although a very useful, relatively minor procedure for use in the poor risk patient with unilateral iliac disease, the result of the study would suggest that the femeorofemoral bypass may not be the best option, from a hæmodynamic point of view, in those patients in whom an iliofemoral reconstruction might alternatively be carried out.

Resting values for carotid blood flow were made in normal subjects and in patients with ultrasonic and radiological evidence of internal carotid artery stenosis. It was found that a luminal stenosis of greater than 75% was required before reduction of blood flow occured. Hypo- and hypercapnia produced reproducibly measureable changes in internal carotid blood flow, but these studies were difficult to perform, requiring considerable subject co-operation, and are unlikely to prove suitable for development as clinical tests. Carotid endarterectomy produced a rise in common and internal carotid blood flow in 12 of 15 patients studied. Even those 3 patients in whom the volume of blood flow was not improved by surgery were rendered asymptomatic, however, suggesting that the cause of symptoms is not reduced blood flow, and that an embolic source had been removed.

The present study has demonstrated the usefulness of ultrasonically-measured flow measurements, both for physiological studies and for routine clinical use. Certainly, the technique can unreservedly be recommended for the routine follow-up of patients with femoropopliteal and femorofemoral bypasses. The duplex scanner is already well established in the evaluation of carotid artery disease, and the extension of the technique to provide flow measurements can only broaden its value. The value of flow measurements in the evaluation of patients with symptoms of arterial disease is less clear. Further studies of patients with peripheral vascular disease at various levels may help to clarify this matter. Whatever method is used to assess the lower limb circulation, the value of measurements made at rest is considerably enhanced with those made during enhanced blood flow.

As with any new technique, the best results are obtained by a conscientious and experienced observer; it takes many months of practise to produce the best images of blood vessels and to recognise and record those signals most suitable for analysis. It is likely that many of the factors contributing to difficulties in usage and to observer error will be further reduced by technological advances, so improving the imaging facility and the accuracy and reproducibility of flow measurements. The present study confirms that the duplex ultrasound scanner has an expanding rôle in non-invasive arterial assessment, and demonstrates that flow measurements made using this technique are of value in the follow-up assessments of patients with arterial reconstructions.

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Appendix I

<u>The measurement of blood flow velocity by Doppler ultrasound</u>

As pointed out in Chapter Two (p 16) ultrasound, reflected by moving blood cells and received by a velocimeter transducer, undergoes 2 shifts in frequency according to the Doppler effect.

The frequency of the ultrasound received by the blood cells, f_R, is given by:

$$f_R = f_s + V_R/\lambda_S$$

where f_S = transmitted frequency of ultrasound
V_R = velocity of receiver resolved in the direction of the source
λ_S = wavelength of the transmitted ultrasound

but $\lambda_S = C/f_S$

where C = velocity of ultrasound in the tissues.

So the first Doppler shift is given by:

$$f_R - f_S = f_S.\ V_R/C$$

A second frequency shift occurs between the blood cells, which act as moving sources of ultrasound of frequency f_R, and the receiving transducer. The frequency received by the transducer f_R', is given by:

$$f_R' = f_R + f_R.\ V_S/C$$

where V_S = velocity of the blood vessel source resolved in the direction of the receiver.

So that $f_R' = f_S + V_R/\lambda_S + V_S/C.\ (f_S + V_R/\lambda_S)$

$$= (1 + V_S/C).\ (1 + VR/C).\ f_S$$

$$= f_S + f_S.\ V_R/C + f_S.\ V_S/C + f_S.\ V_R.\ V_S/C^2$$

But $|V_R| = |V_S| = V$, Where V is the red blood cell velocity

and $V << C$, such that $(V/C)^2 \rightarrow 0$

therefore $f_R' = f_S + 2.\ f_S.\ V/C$

The Doppler shift, f_D, between the transmitted and received signals $(f_R' - f_S)$ is therefore given by:

$$f_R' - f_S = f_D = f_S.\ 2V/C$$

If the ultrasonic beam subtends an angle θ with the direction of the moving blood cells, then the actual blood cell velocity, v, is related to the velocity component in the direction of the ultrasound, V, by:

$$v = V/\cos\theta$$

therefore $f_D = 2v.\cos\theta.\ f_s/C$ (1)

Thus the frequency shift, f_D, is proportional to the blood cell velocity, if f_s and θ are kept constant.

Appendix II

The measurement of blood flow velocity

The blood flow rate, Q_i, through an element of the blood vessel cross section, ΔA_i, is given by:

$$Q_i = v_i.\ \Delta A_i$$

where v_i is the vector blood velocity at that point.

The total blood flow across the whole cross section of the blood vessel, Q, is therefore given by:

$$Q = \Sigma_i Q_i = \Sigma_i (v_i.\ \Delta A_i) \qquad (2)$$

Or, if ΔA_i tends towards infinite smallness (dA):

$$Q = \int_A v.\ dA$$

That is $Q = \bar{v}.\ A$ (3)

where $\bar{v}$ is the spatial average blood flow velocity over the whole cross section

A is the whole cross sectional area.

Appendix III

The Technicare Autosector scanner- Technical aspects

Imaging Mode

Type	Sector
Scan rate	15 or 25 frames/sec
Image plane dimensions	45.5° or 91° sector angle
Maximum pulse repetition rate	3 kHz
Single image formation time	40 or 66 msec
Axial resolution	7.5 MHz: 0.3 mm 10.0 MHz: 0.2 mm
Lateral resolution	7.5 MHz: 1.0 mm 10.0 MHz: 0.8 mm
Fields of view	5-20 cm in 1 cm increments
Beam width (max.; min.)	0.6 x 0.6; 0.4 x 0.4 cm
Focal length (max.; min.)	2.3; 1.3 cm
Depth of focus (max.; min.)	4.5; 3.5 cm

Single gate pulsed Doppler mode

Probe	Mechanical sector
Transducer configuration	Dual element
Transducer centre frequency	4.5 MHz
Beam position	-45° to +45°
Gate ranges	1, 2, 4 and 8 mm
Pulse repetition frequency	6, 7.5, 10, 15 or 30 kHz
Beam width (max.; min.)	1.0 x 1.0; 0.7 x 0.7 cm
Focal length (max.; min.)	2.5; 1.9 cm
Depth of focus (max.; min.)	6; 4 cm

Continuous wave Doppler mode

Probe	Mechanical sector
Transducer configuration	Dual element
Beam position	-45° to +45°
Beam width (max.; min.)	1.0 x 1.0; 0.7 x 0.7 cm
Focal length (max.; min.)	2.5; 1.9 cm
Depth of focus (max.; min.)	6; 4 cm

Spectral display

60 Hz update rate
128 samples
Bidirectional Analysis

Appendix IV

Statistical tests used in the thesis

Mann Whitney *U* test

This is used to test the null hypothesis H_0 that two independent groups have been drawn from the same population. Let n_1 be the number of cases in the smaller group and n_2 in the larger. The data from each group are combined and ranked; the lowest rank is assigned to the algebraically smallest number. If the sum of the ranks assigned to data from the smaller group is R_1, then U is given by:

$$U = n_1 n_2 + \frac{n_1(n_1 + 1)}{2} - R_1$$

As n_1 and n_2 increase in size, the sampling distribution of U rapidly approaches the normal distribution. So, when $n_2 > 20$, the significance of an observed value of U may be determined by:

$$z = \frac{U - \dfrac{n_1 n_2}{2}}{\sqrt{\dfrac{(n_1)(n_2)(n_1 + n_2 + 1)}{12}}}$$

The sampling distribution of U under H_0 is known, so the probability associated with the occurrence under H_0 of any U or z as extreme as an observed value of U or z can thus be determined.

Kruskal-Wallis one-way analysis of variance

This analysis is used to test the null hypothesis that k independent samples come from the same population. As in the Mann Whitney U test the data are combined and ranks assigned. If n_j is the number of data in the j-th sample, R_j the sum of ranks in the j-th sample and $\Sigma\ nj$ the number of data in all samples combined, then H (the statistic used in this analysis) is given by:

$$H + \frac{12}{N(N + 1)} \sum_{j=1}^{k} \frac{Rj^2}{nj} - 3(N + 1)$$

Provided $n_j > 5$, H is distributed approximately as X^2 with $k - 1$ degrees of freedom.

The Spearman Rank correlation coefficient: r_s

This coefficient is a measure of association between two sets of N data which are ranked in ordered series. If the differences between the numerical ranks, d, are calculated for each pair of data, then the coefficient of correlation is given by:

$$r_s = 1 - \frac{6 \sum_{i=1}^{N} d_i^2}{N^3 - 1}$$

Provided $N > 10$, the significance of an observed value of r_s may be tested by Student's t test, with $N - 2$ degrees of freedom:

$$t = r_s \sqrt{\frac{N - 2}{1 - r_s^2}}$$

The tests are described and discussed in great detail by Siegel (1956).